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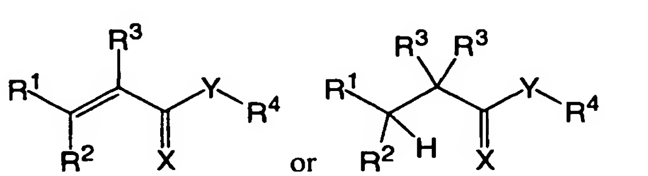

(I)

(57) Abstract: Compounds having the general structure (formule 1) and compositions containing them, for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, , general inflammation arthritis, rheumatic diseases, osteorthritis, inflammatory bowel disorders, inflammatory eye disorders,inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathy pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentiation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders.

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For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

VANILLOID RECEPTOR LIGANDS AND THEIR USE IN TREATMENTS

This application claims the benefit of U.S. Provisional Application Nos. 60/339,161 filed December 10, 2001, 60/344,737, filed December 21, 2001, 60/383,331, filed May 22, 2002 and 60/402,422, filed August 8, 2002, which are hereby incorporated by reference.

Background

The vanilloid receptor 1 (VR1) is the molecular target of capsaicin, the active ingredient in hot peppers. Julius et al. reported the molecular cloning of VR1 (Caterina et al., 1997). VR1 is a non-selective cation channel which is activated or sensitized by a series of different stimuli including capsaicin and resiniferatoxin (exogenous activators), heat & acid stimulation and products of lipid bilayer metabolism, anandamide (Premkumar et al., 2000, Szabo et al., 2000, Gauldie et al., 2001, Olah et al., 2001) and lipoxygenase metabolites (Hwang et al., 2000). VR1 is highly expressed in primary sensory neurons (Caterina et al., 1997) in rats, mice and humans (Onozawa et al., 2000, Mezey et al., 2000, Helliwell et al., 1998, Cortright et al., 2001). These sensory neurons innervate many visceral organs including the dermis, bones, bladder, gastrointestinal tract and lungs; VR1 is also expressed in other neuronal and non-neuronal tissues including but not limited to, CNS nuclei, kidney, stomach and T-cells (Nozawa et al., 2001, Yiangou et al., 2001, Birder et al., 2001). Presumably expression in these various cells and organs may contribute to their basic properties such as cellular signaling and cell division.

Prior to the molecular cloning of VR1, experimentation with capsaicin indicated the presence of a capsaicin sensitive receptor, which could increase the activity of sensory neurons in humans, rats and mice (Holzer, 1991; Dray, 1992, Szallasi and Blumberg 1996, 1999). The results of acute activation by capsaicin in humans was pain at injection site and in other species increased behavioral sensitivity to sensory stimuli (Szallasi and Blumberg, 1999). Capsaicin application to the skin in humans causes a painful reaction characterized not only by the perception of heat and pain at the site of administration but also by a wider area of hyperalgesia and allodynia, two characteristic symptoms of the human

condition of neuropathic pain (Holzer, 1991). Taken together, it seems likely that increased activity of VR1 plays a significant role in the establishment and maintenance of pain conditions. Topical or intradermal injection of capsaicin has also been shown to produce localized vasodilation and edema production (Szallasi and Blumberg 1999, Singh et al., 2001). This evidence indicates that capsaicin through it's activation of VR1 can regulate afferent and efferent function of sensory nerves. Sensory nerve involvement in diseases could therefore be modified by molecules which effect the function of the vanilloid receptor to increase or decrease the activity of sensory nerves.

VR1 gene knockout mice have been shown to have reduced sensory sensitivity to thermal and acid stimuli (Caterina et al., 2000)). This supports the concept that VR1 contributes not only to generation of pain responses (i.e. via thermal, acid or capsaicin stimuli) but also to the maintenance of basal activity of sensory nerves. This evidence agrees with studies demonstrating capsaicin sensitive nerve involvement in disease. Primary sensory nerves in humans and other species can be made inactive by continued capsaicin stimulation. This paradigm causes receptor activation induced desensitization of the primary sensory nerve - such reduction in sensory nerve activity *in vivo* makes subjects less sensitive to subsequent painful stimuli. In this regard both capsaicin and resinferatoxin (exogenous activators of VR1), produce desensitization and they have been used for many proof of concept studies in *in vivo* models of disease (Holzer, 1991, Dray 1992, Szallasi and Blumberg 1999).

VR1 agonists or antagonists have use as analgesics for the treatment of pain of various genesis or aetiology, for example acute, inflammatory and neuropathic pain, dental pain and headache, particularly vascular headache such as migraine, cluster headache and mixed vascular syndromes as well as non-vascular, tension headache. They are also useful as anti-inflammatory agents for the treatment of inflammatory diseases or conditions, for example the treatment of arthritis and rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders (e.g. uvetis), inflammatory or unstable bladder disorders (e.g. cystitis and urinary incontinence), psoriasis and skin complaints with inflammatory components, as well as other chronic inflammatory conditions.

They are, in particular, useful in the treatment of inflammatory pain and associated hyperalgesia and allodynia. They are also useful in the treatment of neuropathic pain and associated hyperalgesia and allodynia, e.g. trigeminal or herpetic neuralgia, diabetic neuropathy pain, causalgia, sympathetically maintained pain and deafferentation syndromes such as brachial plexus avulsion. They are also indicated for the use in the prophylactic or curative treatment of asthma, of epithelial tissue damage or dysfunction, e.g. spontaneous lesions, of herpes simplex, and in the control of disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular e.g. for treating wounds, burns, allergic skin reactions, pruritis and vitiligo, for the prophylactic or curative treatment of gastrointestinal disorders such as gastric ulceration, duodenal ulcers, inflammatory bowel disease and diarrhea, gastric lesions induced by necrotising agents, for example ethanol or chemotherapeutic agents, hair growth, for the treatment of vasomotor or allergic rhinitis and for the treatment of bronchial disorders or bladder disorders, such as bladder hyper-reflexia.

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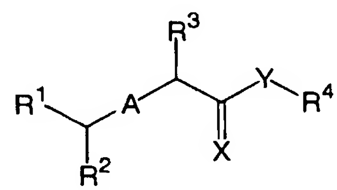
Summary

The present invention comprises a new class of compounds useful in the treatment of diseases, such as vanilloid-receptor-mediated diseases and other maladies, such as inflammatory or neuropathic pain and diseases involving sensory nerve function such as asthma, rheumatoid arthritis, osteoarthritis, inflammatory bowel disorders, urinary incontinence, migraine and psoriasis. In particular, the compounds of the invention are useful for the treatment of acute,

inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders. Analogously, the invention also comprises pharmaceutical compositions comprising the compounds, methods for the treatment of vanilloid-receptor-mediated diseases, such as inflammatory or neuropathic pain, asthma, rheumatoid arthritis, osteoarthritis, inflammatory bowel disorders, urinary incontinence, migraine and psoriasis diseases, using the compounds and compositions of the invention, and intermediates and processes useful for the preparation of the compounds of the invention.

The compounds of the invention are represented by the following general structure

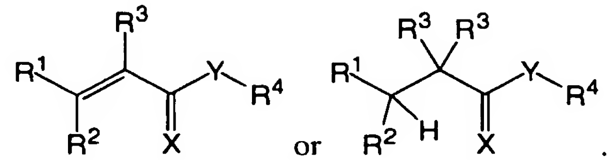


or a pharmaceutically acceptable salt thereof, wherein A, R^1, R^2, R^3, R^4, X and Y are defined below.

The foregoing merely summarizes certain aspects of the invention and is not intended, nor should it be construed, as limiting the invention in any way. All patents, patent applications and other publications recited herein are hereby incorporated by reference in their entirety.

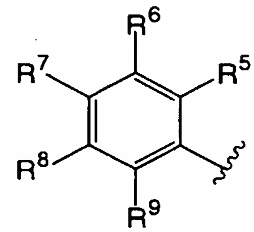
Detailed Description

One aspect of the current invention relates to compounds having the general structure:



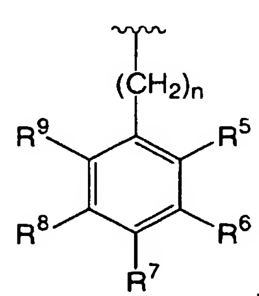
wherein:

R^1 is



or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

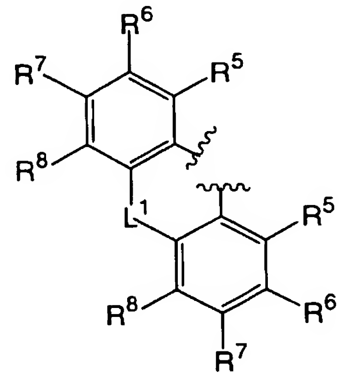
R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},



or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a

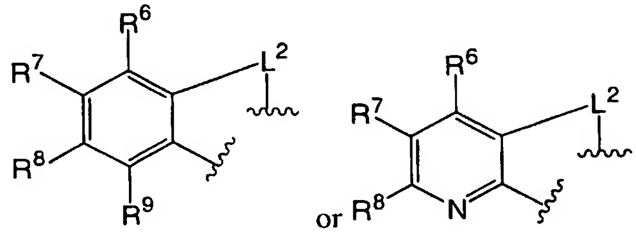
phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

or R^1 and R^2 together are

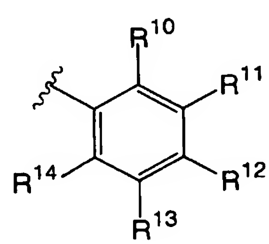


;

R^3 is H or C_{1-4}alkyl; or R^1 and R^3 together are



R^4 is



; or

R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}alkylNR^aR^a$,

$-NR^a$-C_{1-6}alkylOR^a, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)NR^aC_{1-6}alkyl and -NR^{a}C(=O)C_{1-6}alkyl; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^{a}R^a, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O; except that when R^1 is 4-chlorophenyl, 3-bromophenyl, 3-nitrophenyl, 2-nitro-3-chlorophenyl, 3,4-methylenedioxyphenyl, 3-methylthiophenyl or 2,3,4-methoxyphenyl, then R^4 is not phenyl substituted by 1 or 2 substituents selected from halo and C_{1-4}alkyl; and R^1 and R^4 are not both 3,4-methylenedioxyphenyl; and when R^1 is 4-trifluoromethylphenyl, then R^4 is not pyridinyl, 2-methyl-4-aminoquinolinyl or 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl;

R^5 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{a}R^a, -O-C_{1-6}alkylOR^a, -NR^{a}R^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^{a}R^a or -NR^a-C_{1-6}alkylOR^a; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S;

R^6 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{a}R^a, -O-C_{1-6}alkylOR^a, -NR^{a}R^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^{a}R^a or -NR^a-C_{1-6}alkylOR^a; or R^5 and R^6 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-6}alkyl, (=O), -OC_{1-6}alkyl, -NR^aC_{1-6}alkyl, -C_{1-6}alkylOR^a and C_{1-6}alkylNR^{a}R^a, and the available N atoms of the bridge are substituted by R^a, -C_{1-6}alkylOR^a or C_{1-6}alkylNR^{a}R^a;

R^7 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{a}R^a, -O-C_{1-6}alkylOR^a, -NR^{a}R^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^{a}R^a or -NR^a-C_{1-6}alkylOR^a;

R^8 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a; or R^7 and R^8 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-6}alkyl, (=O), -O-C_{1-6}alkyl, -N$R^a$$C_{1-6}$alkyl, -$C_{1-6}$alkylO$R^a$ and C_{1-6}alkylNR^aR^a, and the available N atoms of the bridge are substituted by R^a, -C_{1-6}alkylOR^a or C_{1-6}alkylNR^aR^a;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a;

R^{10} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkylN$R^aR^a$, -O-$C_{1-6}$alkylO$R^a$, -O-$C_{1-6}$alkylC(=O)O$R^a$, -N$R^aR^a$, -N$R^a$-$C_{1-4}$haloalkyl, -N$R^a$-$C_{1-6}$alkylN$R^aR^a$, -N$R^a$-$C_{1-6}$alkylO$R^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)N$R^a$$C_{1-6}$alkyl or -N$R^a$C(=O)$C_{1-6}$alkyl;

R^{11} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkylN$R^aR^a$, -O-$C_{1-6}$alkyl$R^c$, -O-$C_{1-6}$alkylO$R^a$, -O-$C_{1-6}$alkylC(=O)O$R^a$, -N$R^aR^a$, -N$R^a$-$C_{1-4}$haloalkyl, -N$R^a$-$C_{1-6}$alkylN$R^aR^a$, -N$R^a$-$C_{1-6}$alkylO$R^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)N$R^a$$C_{1-6}$alkyl or -N$R^a$C(=O)$C_{1-6}$alkyl; or R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^aR^a, -C_{1-6}alkylNR^aR^a, -C(=O)OR^a, -C(=O)NR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -OC(=O)C_{1-6}alkyl, -NR^aC(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a,

$-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^aR^a, $-C_{1-3}$alkyl$C(=O)OR^a$, $-C_{1-3}$alkyl$C(=O)NR^aR^a$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^aC(=O)C_{1-6}$alkyl, $-C(=O)R^c$ or $-C_{1-3}$alkylR^c; wherein if R^{10}, R^{12}, R^{13} and R^{14} are all H, then R^{11} is not $-O-C_{1-6}$alkylNR^aR^a or $-O-C_{1-6}$alkylOR^a;

R^{12} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl; or R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}$alkylOR^a, $-C_{1-6}$alkyl, $-NR^aR^a$, $-C_{1-6}$alkylNR^aR^a, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}$alkyl$C(=O)OR^a$, $-C_{1-3}$alkyl$C(=O)NR^aR^a$, $-OC(=O)C_{1-6}$alkyl, $-NR^aC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl or $-C_{1-3}$alkyl$NR^aC(=O)C_{1-6}$alkyl, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^a, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^aR^a, $-C_{1-3}$alkyl$C(=O)OR^a$, $-C_{1-3}$alkyl$C(=O)NR^aR^a$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^aC(=O)C_{1-6}$alkyl, $-C(=O)R^c$ or $-C_{1-3}$alkylR^c;

when R^1 is 4-C_{1-6}alkylphenyl or 2,4-dimethylphenyl, then R^{11} is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylR^c, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl; or R^{10} and R^{11} together are $-L^3-NR^a-$, respectively, or $-L^4-O-$, respectively; or R^{11} and R^{12} are $-NR^a-L^3-$, $-L^3-NR^a-$, $-O-L^4-$ or $-L^4-O-$; or R^{12} is $-NR^aR^b$; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O; or R^4 is a saturated

or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 1, 2 or 3 substituents independently selected from C_{2-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl and $-NR^aC(=O)C_{1-6}$alkyl;

R^{13} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

R^{14} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

R^a is independently, at each instance, H, phenyl, benzyl or C_{1-6}alkyl;

R^b is H, C_{1-6}alkyl, $-C(=O)C_{1-6}$alkyl, C_{1-6}alkyl-O-R^a;

R^c is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-3}haloalkyl, $-OR^a$ and $-NR^aR^a$; or R^c is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the

heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-3}haloalkyl, $-OR^a$ and $-NR^aR^a$;

L^1 is a bond, $-CH_2CH_2-$ or $-CH=CH-$;

L^2 is NR^a, O, $S(=O)_n$, $-N=CH-$, $-CH_2NR^a-$, $-CH=N-$ or $-NR^aCH_2-$;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

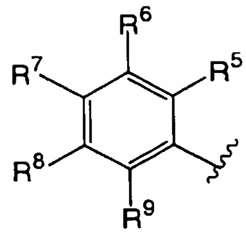
L^4 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0 or 1 atoms independently selected from O, N and S, wherein at least one of the carbon atoms in the bridge is substituted by =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OC_{1-6}alkyl$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

X is O, S or NR^a; or X and R^2 together are $=N-CH=CH-$, $=C-O-$, $=C-S-$, or $=C-NR^a-$;

Y is NH or O; and

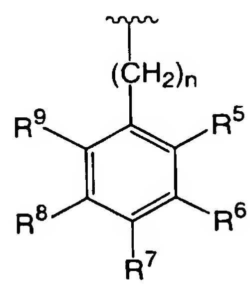
n is independently, at each instance, 0, 1 or 2; with the proviso that when R^1 is 4-chlorophenyl, then R^4 is not 3-methoxyphenyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},

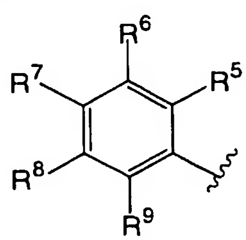


,

or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7; and

R^3 is H or C_{1-4}alkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



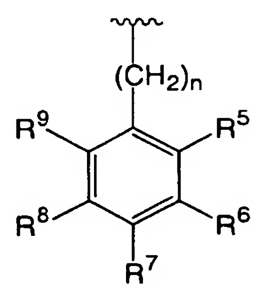
.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is independently, at each instance, C_{2-9}alkyl or C_{1-4}haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

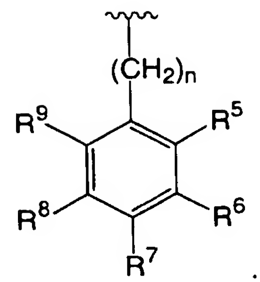
In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is



,

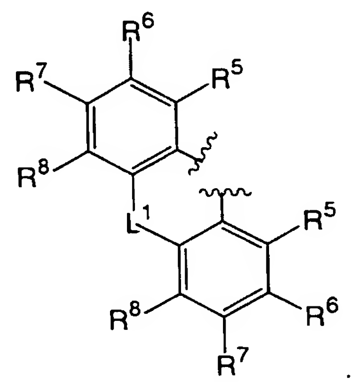
or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is

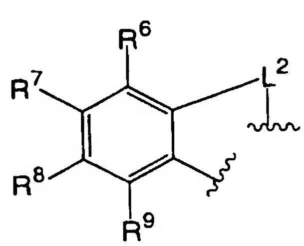


In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

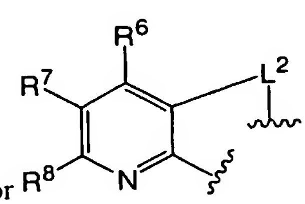
In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 and R^2 together are



In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 and R^3 together are

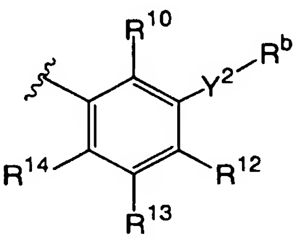


or



In another embodiment, in conjunction with the novel compound embodiments above and below, X and R^2 together are =N-CH=CH-, =C-O-, =C-S-, or =C-NR^a-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is

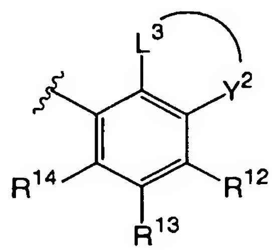


;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^a- or -O-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



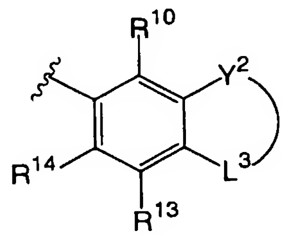
;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0 or 1 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^aR^a, -C_{1-6}alkylNR^aR^a, -C(=O)OR^a, -C(=O)NR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -OC(=O)C_{1-6}alkyl, -NR^aC(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, -C(=O)R^c or -C_{1-3}alkylR^c;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^b- or -O-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



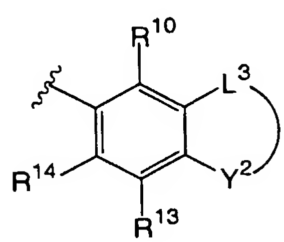
;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl\text{-}O\text{-}R^a$; and

Y^2 is $-NR^b-$ or -O-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



;

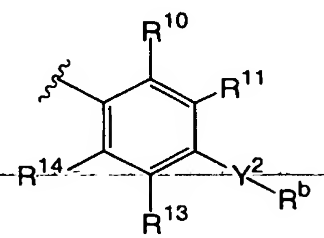
L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$,

and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^{a}R^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^{a}R^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^{a}C(=O)C_{1-6}alkyl, -C(=O)R^c or -C_{1-3}alkylR^c;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^b- or -O-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



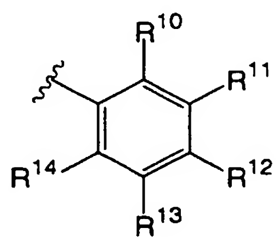
;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^a- or -O-.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^{a}R^a, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



;

R^{10} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkylNR^{a}R^a, -O-$C_{1-6}$alkylOR^a, -O-$C_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^{a}R^a, -NR^a-C_{1-6}alkylOR^a, -C(=O)C_{1-6}alkyl,

$-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

R^{11} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylR^c, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

C_{1-6}alkylNR^aR^a;

R^{12} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

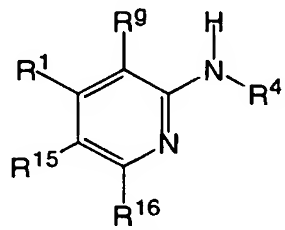
R^{13} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl; and

R^{14} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl; wherein one of R^{10} and R^{12} is not H.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused

phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}haloalkyl, $-OR^a$ and $-NR^aR^a$.

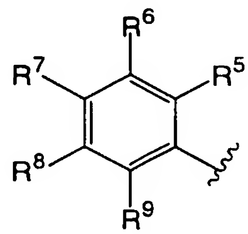
Another aspect of the invention relates to a compound having the structure:



or any pharmaceutically-acceptable salt thereof, wherein:

n is independently, at each instance, 0, 1 or 2.

R^1 is



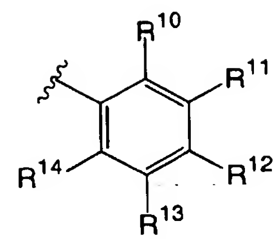
;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl or C_{1-3}alkyl;

R^4 is



; or

R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, oxo, $-OR^d$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-OC_{1-6}$alkyl$C(=O)OR^d$, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^dC_{1-6}$alkyl and $-NR^dC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^d, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^dR^d, $-C_{1-3}$alkyl$C(=O)OR^d$, $-C_{1-3}$alkyl$C(=O)NR^dR^d$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^dC(=O)C_{1-6}$alkyl, $-C(=O)R^f$ or $-C_{1-3}$alkylR^f; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl;

R^5 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, naphthyl, $-CO_2(C_{1-6}$alkyl), $-C(=O)(C_{1-6}$alkyl), $-C(=O)NR^dR^d$, $-NR^dC(=O)R^d$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}$alkyl), $-C_{1-8}$alkylOR^d, $-C_{1-6}$alkylNR^dR^d,

$-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$, $-OC(=O)NR^dR^d$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(C_{1-6}alkyl)$, a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$ or $-S(C_{1-6}alkyl)$; or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, $C_{1-2}haloalkyl$ and $C_{1-3}alkyl$;

R^8 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(C_{1-6}alkyl)$, a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)(C_{1-6}alkyl)$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$,

$-NR^dS(=O)_2(C_{1-6}alkyl)$, $-OC(=O)NR^dR^d$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-4}$haloalkyl, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$ or $-S(C_{1-6}alkyl)$;

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$,

$-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^{11} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{11} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$,

$-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{11} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$;

R^{12} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$,

$-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{12} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{12} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; wherein if R^{11} or R^{13} is CF_3, then R^{12} is not F; or R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long

as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^dR^d$, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^dR^d, -N(R^d)C(=NR^d)NR^dR^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2NR^dR^d$, -NR^dC_{2-6}alkylNR^dR^d and -NR^dC_{2-6}alkylOR^d, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^d, -C_{1-6}alkyl, -C_{1-6}alkylNR^dR^d, -C_{1-3}alkylC(=O)OR^d, -C_{1-3}alkylC(=O)NR^dR^d, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl, -C(=O)R^f or -C_{1-3}alkylR^f;

R^{13} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^dR^d$, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^dR^d, -N(R^d)C(=NR^d)NR^dR^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2NR^dR^d$, -NR^dC_{2-6}alkylNR^dR^d and -NR^dC_{2-6}alkylOR^d; or R^{13} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl),

$-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{13} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^{14} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{14} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$,

$-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{14} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^d is independently, at each instance, H, phenyl, benzyl or $C_{1-6}alkyl$;

R^e is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-4-yl, 1,2,4-triazol-4-yl, 1,2,4-triazol-5-yl, isoxazol-3-yl, isoxazol-5-yl, pyrazol-3-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-

oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazoline, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,, 2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazole, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine, 1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine, 1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-

tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 2,3-dihydropyrimidine, 2,5-dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine, 1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1,2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-

1,3,4-oxadiazine and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^f is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; or R^f is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; and

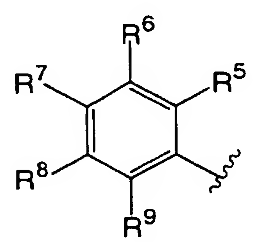
~~R^g is hydrogen or $-CH_3$;~~

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{16} is halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl or C_{1-3}alkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{10} is independently, at each instance, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro,

$-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



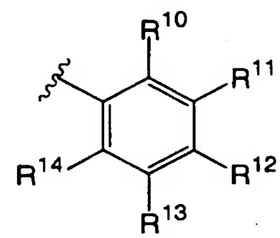
In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is $C_{1-5}alkyl$, halo or $C_{1-4}haloalkyl$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is R^e substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



In another embodiment, in conjunction with the novel compound embodiments above and below, R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^dR^d$, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^dR^d, -N(R^d)C(=NR^d)NR^dR^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2NR^dR^d$, -NR^dC_{2-6}alkylNR^dR^d and -NR^dC_{2-6}alkylOR^d, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^d, -C_{1-6}alkyl, -C_{1-6}alkylNR^dR^d, -C_{1-3}alkylC(=O)OR^d, -C_{1-3}alkylC(=O)NR^dR^d, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl, -C(=O)R^f or -C_{1-3}alkylR^f; or

R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl),

$-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, oxo, $-OR^d$, $-S(=O)_nC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-OC_{1-6}alkylC(=O)OR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^dC_{1-6}alkyl$ and $-NR^dC(=O)C_{1-6}alkyl$; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$.

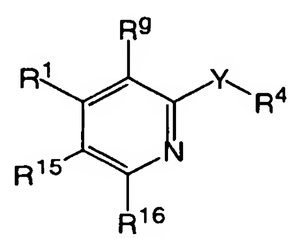
In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms

being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, oxo, $-OR^d$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-OC_{1-6}$alkyl$C(=O)OR^d$, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^dC_{1-6}$alkyl and $-NR^dC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^d, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^dR^d, $-C_{1-3}$alkyl$C(=O)OR^d$, $-C_{1-3}$alkyl$C(=O)NR^dR^d$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^dC(=O)C_{1-6}$alkyl, $-C(=O)R^f$ or $-C_{1-3}$alkylR^f.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O.

Another aspect of the invention relates to a compound having the structure:



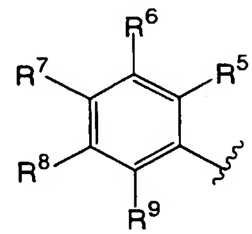
or any pharmaceutically-acceptable salt thereof, wherein:

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

Y is NH, O or S;

R^1 is



;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^c substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl or C_{1-3}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$,

$-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl;

R^5 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, naphthyl, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)R^d$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$, $-OC(=O)NR^dR^d$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle

containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d or -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d, -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d or -S(C_{1-6}alkyl); or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^8 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d, -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d or -NR^dC_{2-6}alkylOR^d, -CO_2(C_{1-6}alkyl), -C(=O)(C_{1-6}alkyl), -C(=O)NR^dR^d, -NR^dC(=O)(C_{1-6}alkyl), -NR^dC(=O)NR^dR^d, -NR^dCO_2(C_{1-6}alkyl), -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d, -S(=O)$_n$(C_{1-6}alkyl), -S(=O)$_2NR^dR^d$, -NR^dS(=O)$_2$(C_{1-6}alkyl), -OC(=O)NR^dR^d or a -$(CR^qR^q)_o$phenyl wherein the phenyl is substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is -$(CR^qR^q)_o$Het wherein Het is a saturated or unsaturated

5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d, -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d or -S(C_{1-6}alkyl);

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^dR^d$, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^dR^d, -N(R^d)C(=NR^d)NR^dR^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2NR^dR^d$, -NR^dC_{2-6}alkylNR^dR^d and -NR^dC_{2-6}alkylOR^d; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^dR^d$, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^dR^d, -N(R^d)C(=NR^d)NR^dR^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2NR^dR^d$, -NR^dC_{2-6}alkylNR^dR^d and

$-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^d is independently, at each instance, H, phenyl, benzyl or $C_{1-6}alkyl$;

R^e is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-4-yl, 1,2,4-triazol-4-yl, 1,2,4-triazol-5-yl, isoxazol-3-yl, isoxazol-5-yl, pyrazol-3-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazoline, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,,

2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazole, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine, 1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine, 1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-

[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 2,3-dihydropyrimidine, 2,5-dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine, 1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1,2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-1,3,4-oxadiazine and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^f is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; or R^f is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently

selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$;

R^g is hydrogen or $-CH_3$;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

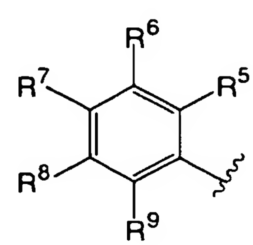
R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is S.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-5}alkyl, halo or C_{1-4}haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5;

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered

monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{16} is, independently, in each instance, halo, $-NH_2$, $-NHC_{1-3}alkyl$, $-N(C_{1-3}alkyl)C_{1-3}alkyl$ or C_{1-3}alkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is an unsaturated 6-membered ring containing 0 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0,

1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S that is vicinally fused

with a saturated or unsaturated 3- or 4-atom bridge containing 0 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, ~~$-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$,~~ $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s; and the ring and

bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 6-membered ring containing 0 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$,

$-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

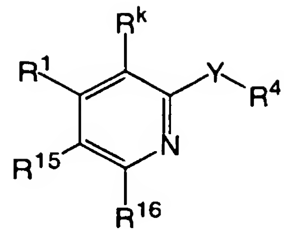
In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is independently, at each instance, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)(C_{1-6}alkyl)$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$ or $-OC(=O)NR^dR^d$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is a $-(CR^qR^q)_o$phenyl wherein the phenyl is substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is $-(CR^qR^q)_o$Het wherein Het is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, $C_{1-2}haloalkyl$ and $C_{1-3}alkyl$.

Another aspect of the invention relates to a compound having the structure:

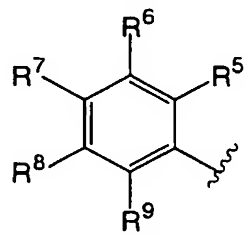


or any pharmaceutically-acceptable salt thereof, wherein:

Y is O or S;

n is independently, at each instance, 0, 1 or 2.

R^1 is



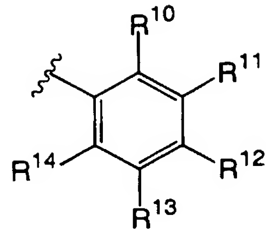
;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^i substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, the heterocycle and bridge being substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl, $-OC_{1-3}$alkyl, $-C_{1-2}$haloalkyl, $-OC_{1-2}$haloalkyl or C_{1-3}alkyl;

R^4 is



;

wherein when R^1 is bromophenyl, methylphenyl or trifluoromethylphenyl, R^4 is not trifluoromethylphenyl or trifluoromethylhalophenyl; or R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and each of the available nitrogen atoms in the heterocycle are substituted by H, $-C_{1-6}$alkylOR^h, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^hR^h, $-C_{1-3}$alkyl$C(=O)OR^h$, $-C_{1-3}$alkyl$C(=O)NR^hR^h$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}$alkylR^j; or R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 0, 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms selected from S and O with the remainder being carbon atoms, wherein each of the carbon atoms of the ring is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the ring are substituted by H, $-C_{1-6}$alkylOR^h, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^hR^h, $-C_{1-3}$alkyl$C(=O)OR^h$, $-C_{1-3}$alkyl$C(=O)NR^hR^h$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}$alkylR^j;

R^5 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, nitro, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -NR^{h}R^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^{h}R^h, -NR^hC_{2-6}alkylOR^h, naphthyl, -CO_2(C_{1-6}alkyl), -C(=O)(C_{1-6}alkyl), -C(=O)NR^{h}R^h, -NR^{h}C(=O)R^h, -NR^{h}C(=O)NR^{h}R^h, -NR^hCO_2(C_{1-6}alkyl), -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^{h}R^h, -S(=O)$_n$(C_{1-6}alkyl), -S(=O)$_2$NR^{h}R^h, -NR^{h}S(=O)$_2$(C_{1-6}alkyl), -OC(=O)NR^{h}R^h, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -NR^{h}R^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^{h}R^h or -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^{h}R^h, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, bromo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -NR^{h}R^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^{h}R^h, -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^{h}R^h or -S(C_{1-6}alkyl); or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^8 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -NR^{h}R^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^{h}R^h, -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^{h}R^h, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, nitro, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -N$R^h$$C_{1-4}$haloalkyl, -N$R^h$$C_{2-6}$alkylN$R^hR^h$ or -N$R^h$$C_{2-6}$alkylO$R^h$, -$CO_2$($C_{1-6}$alkyl), -C(=O)($C_{1-6}$alkyl), -C(=O)N$R^hR^h$, -N$R^h$C(=O)($C_{1-6}$alkyl), -N$R^h$C(=O)N$R^hR^h$, -N$R^h$$CO_2$($C_{1-6}$alkyl), -$C_{1-8}$alkylO$R^h$, -$C_{1-6}$alkylN$R^hR^h$, -S(=O)$_n$($C_{1-6}$alkyl), -S(=O)$_2NR^hR^h$, -N$R^h$S(=O)$_2$($C_{1-6}$alkyl), -OC(=O)N$R^hR^h$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -N$R^h$$C_{1-4}$haloalkyl, -N$R^h$$C_{2-6}$alkylN$R^hR^h$, -N$R^h$$C_{2-6}$alkylO$R^h$, -$C_{1-8}$alkylO$R^h$, -$C_{1-6}$alkylN$R^hR^h$ or -S(C_{1-6}alkyl); or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^hR^h, -N$R^h$$C_{2-6}$alkylN$R^hR^h$ and -N$R^h$$C_{2-6}$alkylO$R^h$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1 or 2 atoms selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O

and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC$_{2-6}$alkylNR^{h}R^h, -OC$_{2-6}$alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^{h}C$_{2-6}$alkylNR^{h}R^h and -NR^{h}C$_{2-6}$alkylOR^h; or R^{10} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro; -C(=O)(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC$_{2-6}$alkylNR^{h}R^h, -OC$_{2-6}$alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^{h}C$_{2-6}$alkylNR^{h}R^h and -NR^{h}C$_{2-6}$alkylOR^h;

R^{11} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC$_{2-6}$alkylNR^{h}R^h, -OC$_{2-6}$alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^{h}C$_{2-6}$alkylNR^{h}R^h and -NR^{h}C$_{2-6}$alkylOR^h; or R^{11} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo

groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$$NR^hR^h$, -S(=O)$_2$N($R^h$)C(=O)($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)O($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)$NR^hR^h$, -$NR^hR^h$, -N($R^h$)C(=O)($C_{1-8}$alkyl), -N($R^h$)C(=O)O($C_{1-8}$alkyl), -N($R^h$)C(=O)$NR^hR^h$, -N($R^h$)C(=$NR^h$)$NR^hR^h$, -N($R^h$)S(=O)$_2$($C_{1-8}$alkyl), -N($R^h$)S(=O)$_2$$NR^hR^h$, -$NR^hC_{2-6}$alkyl$NR^hR^h$ and -NR^hC_{2-6}alkylOR^h; or R^{11} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$$NR^hR^h$, -S(=O)$_2$N($R^h$)C(=O)($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)O($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)$NR^hR^h$, -$NR^hR^h$, -N($R^h$)C(=O)($C_{1-8}$alkyl), -N($R^h$)C(=O)O($C_{1-8}$alkyl), -N($R^h$)C(=O)$NR^hR^h$, -N($R^h$)C(=$NR^h$)$NR^hR^h$, -N($R^h$)S(=O)$_2$($C_{1-8}$alkyl), -N($R^h$)S(=O)$_2$$NR^hR^h$, -$NR^hC_{2-6}$alkyl$NR^hR^h$ and -NR^hC_{2-6}alkylOR^h;

R^{12} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$$NR^hR^h$, -S(=O)$_2$N($R^h$)C(=O)($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)O($C_{1-8}$alkyl), -S(=O)$_2$N($R^h$)C(=O)$NR^hR^h$, -$NR^hR^h$, -N($R^h$)C(=O)($C_{1-8}$alkyl), -N($R^h$)C(=O)O($C_{1-8}$alkyl), -N($R^h$)C(=O)$NR^hR^h$, -N($R^h$)C(=$NR^h$)$NR^hR^h$, -N($R^h$)S(=O)$_2$($C_{1-8}$alkyl), -N($R^h$)S(=O)$_2$$NR^hR^h$, -$NR^hC_{2-6}$alkyl$NR^hR^h$ and -NR^hC_{2-6}alkylOR^h; or R^{12} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3

atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{12} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h;

R^{13} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{13} is a saturated or unsaturated 5-, 6- or 7-membered

monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{13} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h;

R^{14} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and

$-NR^hC_{2-6}alkylOR^h$; or R^{14} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1 or 2 atoms selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$; or R^{14} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$;

R^h is independently, at each instance, H, phenyl, benzyl or $C_{1-6}alkyl$, the phenyl, benzyl and $C_{1-6}alkyl$ being substituted by 0, 1, 2 or 3 substituents selected from halo, $C_{1-4}alkyl$, $C_{1-3}haloalkyl$, $-OC_{1-4}alkyl$, $-NH_2$, $-NHC_{1-4}alkyl$, $-N(C_{1-4}alkyl)C_{1-4}alkyl$;

R^i is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazol-5-yl, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-

thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-3-yl, imidazol-4-yl, 1,2,4-triazole, 1,2,4-triazole, isoxazole, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazolin-1-yl, 2-imidazolin-2-yl, 2-imidazolin-5-yl, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,, 2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazol-1-yl, 4,5-dihydro-1H-[1,2,3]triazol-3-yl, 4,5-dihydro-1H-[1,2,3]triazol-5-yl, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine, 1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-

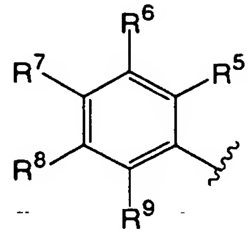
thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine, 1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 1,4-dihydropyrimidin-1-yl, 1,4-dihydropyrimidin-4-yl, 1,4-dihydropyrimidin-5-yl, 1,4-dihydropyrimidin-6-yl,

2,3-dihydropyrimidine, 2,5-dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine, 1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1;2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-1,3,4-oxadiazine, and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^j is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^h$ and $-NR^hR^h$; or R^j is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^h$ and $-NR^hR^h$; and

R^k is hydrogen or $-CH_3$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{2-6}alkyl or C_{1-4}haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is R^i substituted by 1, 2 or 3 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^i is substituted by one substituent selected from halo, C_{1-4}haloalkyl and C_{1-5}alkyl, and additionally by 0, 1 or 2 substituents independently selected from R^5.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is H.

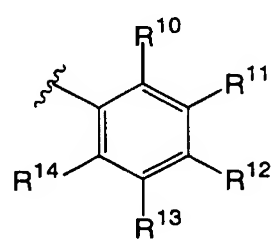
In another embodiment, in conjunction with the novel compound embodiments above and below, R^{15} is R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, the heterocycle and bridge being substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}; or R^{15} is $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$,

$-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, and $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{16} is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{16} is halo, $-NHC_{1-3}alkyl$, $-N(C_{1-3}alkyl)C_{1-3}alkyl$, $-OC_{1-3}alkyl$, $-C_{1-2}haloalkyl$, $-OC_{1-2}haloalkyl$ or $C_{1-3}alkyl$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is



;

wherein at least one of R^{10}, R^{11}, R^{12}, R^{13} and R^{14} is other than $C_{1-4}haloalkyl$ or halo.

In another embodiment, in conjunction with the novel compound embodiments above and below, at least one of R^{10}, R^{11}, R^{12}, R^{13} and R^{14} is $-OR^h$ or $-NR^hR^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-OC_{1-6}alkylC(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the heterocycle are substituted by H, $-C_{1-6}alkylOR^h$, $-C_{1-6}$alkyl, $-C_{1-6}alkylNR^hR^h$, $-C_{1-3}alkylC(=O)OR^h$, $-C_{1-3}alkylC(=O)NR^hR^h$, $-C_{1-3}alkylOC(=O)C_{1-6}$alkyl, $-C_{1-3}alkylNR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}alkylR^j$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1 or 2 atoms selected from O, N and S, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-OC_{1-6}alkylC(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^h$, $-C_{1-6}$alkyl, $-C_{1-6}alkylNR^hR^h$, $-C_{1-3}alkylC(=O)OR^h$, $-C_{1-3}alkylC(=O)NR^hR^h$, $-C_{1-3}alkylOC(=O)C_{1-6}$alkyl, $-C_{1-3}alkylNR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}alkylR^j$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms selected from S and O with the remainder being carbon atoms, wherein each of the carbon atoms of the ring is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$,

$-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the ring are substituted by H, $-C_{1-6}$alkylOR^h, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^hR^h, $-C_{1-3}$alkyl$C(=O)OR^h$, $-C_{1-3}$alkyl$C(=O)NR^hR^h$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}$alkylR^j.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 0, 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms selected from S and O with the remainder being carbon atoms, wherein at least one of the carbon atoms of the ring is substituted by C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^5 and R^9 are each independently selected from H, C_{1-4}haloalkyl, halo, nitro, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-CO_2(C_{1-6}$alkyl$)$, $-C(=O)(C_{1-6}$alkyl$)$, $-C(=O)NR^hR^h$, $-NR^hC(=O)R^h$, $-NR^hC(=O)NR^hR^h$, $-NR^hCO_2(C_{1-6}$alkyl$)$, $-C_{1-8}$alkylOR^h, $-C_{1-6}$alkylNR^hR^h, $-S(=O)_n(C_{1-6}$alkyl$)$, $-S(=O)_2NR^hR^h$, $-NR^hS(=O)_2(C_{1-6}$alkyl$)$ and $-OC(=O)NR^hR^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^6 and R^8 are each independently selected from H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h or $-NR^hC_{2-6}$alkylOR^h, $-C_{1-8}$alkylOR^h, $-C_{1-6}$alkylNR^hR^h and $-S(C_{1-6}$alkyl$)$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is independently, at each instance,

C_{1-8}alkyl, C_{1-4}haloalkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -N$R^h$$C_{1-4}$haloalkyl, -N$R^h$$C_{2-6}$alkylN$R^hR^h$, -N$R^h$$C_{2-6}$alkylO$R^h$, -$C_{1-8}$alkylO$R^h$, -$C_{1-6}$alkylN$R^hR^h$ or -S(C_{1-6}alkyl).

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{10} and R^{14} are each independently selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^hR^h, -N$R^h$$C_{2-6}$alkylN$R^hR^h$ and -N$R^h$$C_{2-6}$alkylO$R^h$ and C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^hR^h, -N$R^h$$C_{2-6}$alkylN$R^hR^h$ and -N$R^h$$C_{2-6}$alkylO$R^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{11} and R^{13} are independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h,

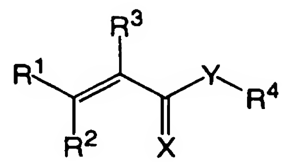
$-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$ and $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^{12} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$; or R^{12} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is S.

Another aspect of the invention relates to a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

R^3 is H or C_{1-4}alkyl;

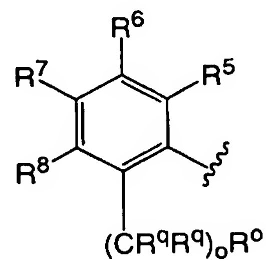
R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$,

-O-C_{1-6}alkylOR^m, -NR^{m}R^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^{m}R^m or -NR^m-C_{1-6}alkylOR^m;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{m}R^m, -O-C_{1-6}alkylOR^m, -NR^{m}R^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^{m}R^m or -NR^m-C_{1-6}alkylOR^m; and

(A) R^1 is



R^2 is H, -OR^m, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC_{2-6}alkylNR^{m}R^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^mC_{2-6}alkylNR^{m}R^m, -NR^mC_{2-6}alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC_{2-6}alkylNR^{m}R^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^mC_{2-6}alkylNR^{m}R^s, -NR^mC_{2-6}alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo,

cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

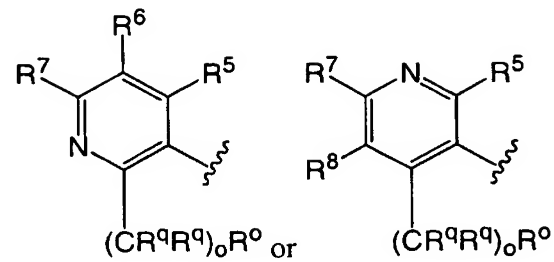
R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

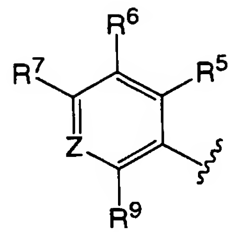
R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$,

$-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

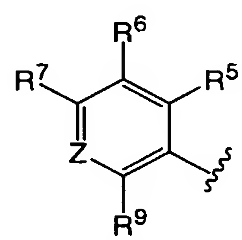
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; or

R^2 is -(C(R^q)$_2$)$_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)N$R^m$$R^m$, -C(=N$R^m$)N$R^m$$R^m$, -O$R^m$, -OC(=O)$R^n$, -OC(=O)N$R^m$$R^m$, -OC(=O)N($R^m$)S(=O)$_2$$R^n$, -O$C_{2-6}$alkylN$R^m$$R^m$, -O$C_{2-6}$alkylO$R^m$, -S$R^m$, -S(=O)$R^n$, -S(=O)$_2$$R^n$, -S(=O)$_2NR^m$$R^m$, -S(=O)$_2$N($R^m$)C(=O)$R^n$, -S(=O)$_2$N($R^m$)C(=O)O$R^n$, -S(=O)$_2$N($R^m$)C(=O)N$R^m$$R^m$, -N$R^m$$R^m$, -N($R^m$)C(=O)$R^n$, -N($R^m$)C(=O)O$R^n$, -N($R^m$)C(=O)N$R^m$$R^m$, -N($R^m$)C(=N$R^m$)N$R^m$$R^m$, -N($R^m$)S(=O)$_2$$R^n$, -N($R^m$)S(=O)$_2NR^m$$R^m$, -N$R^m$$C_{2-6}$alkylN$R^m$$R^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^m$$R^s$, -C(=N$R^m$)N$R^m$$R^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^m$$R^s$, -OC(=O)N($R^m$)S(=O)$_2$$R^s$, -O$C_{2-6}$alkylN$R^m$$R^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2$$R^s$, -S(=O)$_2NR^m$$R^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^m$$R^s$, -N$R^m$$R^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^m$$R^s$, -N($R^m$)C(=N$R^m$)N$R^m$$R^s$, -N($R^m$)S(=O)$_2$$R^s$, -N($R^m$)S(=O)$_2NR^m$$R^s$, -N$R^m$$C_{2-6}$alkylN$R^m$$R^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)N$R^m$$R^m$, -C(=N$R^m$)N$R^m$$R^m$, -O$R^m$, -OC(=O)$R^n$, -OC(=O)N$R^m$$R^m$, -OC(=O)N($R^m$)S(=O)$_2$$R^n$, -O$C_{2-6}$alkylN$R^m$$R^m$, -O$C_{2-6}$alkylO$R^m$, -S$R^m$, -S(=O)$R^n$, -S(=O)$_2$$R^n$, -S(=O)$_2NR^m$$R^m$, -S(=O)$_2$N($R^m$)C(=O)$R^n$, -S(=O)$_2$N($R^m$)C(=O)O$R^n$, -S(=O)$_2$N($R^m$)C(=O)N$R^m$$R^m$, -N$R^m$$R^m$, -N($R^m$)C(=O)$R^n$, -N($R^m$)C(=O)O$R^n$, -N($R^m$)C(=O)N$R^m$$R^m$, -N($R^m$)C(=N$R^m$)N$R^m$$R^m$, -N($R^m$)S(=O)$_2$$R^n$, -N($R^m$)S(=O)$_2NR^m$$R^m$, -N$R^m$$C_{2-6}$alkylN$R^m$$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^m$$R^s$, -C(=N$R^m$)N$R^m$$R^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^m$$R^s$, -OC(=O)N($R^m$)S(=O)$_2$$R^s$, -O$C_{2-6}$alkylN$R^m$$R^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2$$R^s$, -S(=O)$_2NR^m$$R^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^m$$R^s$, -N$R^m$$R^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^m$$R^s$, -N($R^m$)C(=N$R^m$)N$R^m$$R^s$, -N($R^m$)S(=O)$_2$$R^s$, -N($R^m$)S(=O)$_2NR^m$$R^s$, -N$R^m$$C_{2-6}$alkylN$R^m$$R^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and -N$R^m$$C_{2-6}$alkylO$R^m$; or

R^2 is -(C(R^q)$_2$)$_o$$R^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S,

wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected

from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

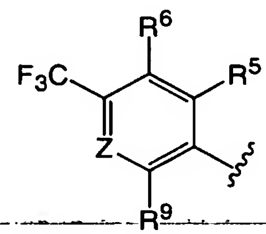
R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, -OR^m, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^n, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2NR^mR^m$, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2NR^mR^m$, -NR^mC_{2-6}alkylNR^mR^m, -NR^mC_{2-6}alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^mR^s, -NR^mR^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^mR^s, -N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)$_2R^s$, -N(R^m)S(=O)$_2NR^mR^s$, -NR^mC_{2-6}alkylNR^mR^s, -NR^mC_{2-6}alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m,

$-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

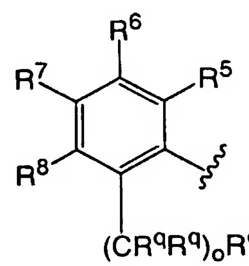
R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, 80, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge

are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$ or -N$R^m$$C_{2-6}$alkylO$R^m$; and

Y is O or NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$,

$-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$,

$-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-NR^mR^m$ or $-NR^m-C_{1-4}$haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-5}alkyl, C_{1-4}haloalkyl, I, Br or Cl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2

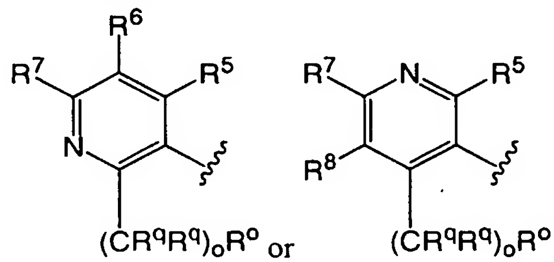
oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$,

$-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; [C_{1-8}alkyl, C_{1-5}haloalkyl, I, Br or Cl]

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo,

cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $\cancel{-N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)_2R^s, -N(R^m)S(=O)_2NR^mR^s,}$ $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-NR^mR^m$ or $-NR^m-C_{1-4}haloalkyl$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, I, Br or Cl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

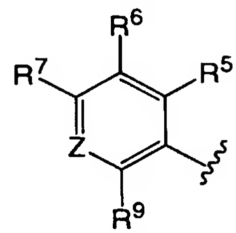
In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon

atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$,

$-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a heterocycle selected from indole, 3H-indole, benzo[b]furan, benzothiophene, 1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 1,2,3,4-tetrahydroquinoline, isoquinoline, cinnoline, phthalazine, quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-9}alkyl$, oxo, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$,

-OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C$_{1-4}$alkyl substituted by 1 or 2 groups selected from C$_{1-2}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m , -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and -NR^{m}C$_{2-6}$alkylOR^m.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a heterocycle selected from 6-indole, 7-indole, 6-3H-indole, 7-3H-indole, 6-benzo[b]furan, 7-benzo[b]furan, 6-benzothiophene, 7-benzothiophene, 6-1H-indazole, 7-1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 7-1,2,3,4-tetrahydroquinoline, 8-1,2,3,4-tetrahydroquinoline, isoquinolin-7-yl, isoquinolin-8-yl, 7-cinnoline, 8-cinnoline, phthalazine, 7-quinazoline, 8-quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C$_{1-9}$alkyl, oxo, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OR^m, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{m}R^m, -O-C$_{1-6}$alkylOR^m, -NR^{m}R^m, -NR^m-C$_{1-4}$haloalkyl, -NR^m-C$_{1-6}$alkylNR^{m}R^m, -NR^m-C$_{1-6}$alkylOR^m, -C(=O)C$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{m}C$_{1-6}$alkyl, -NR^{m}C(=O)C$_{1-6}$alkyl -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s,

$-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$.

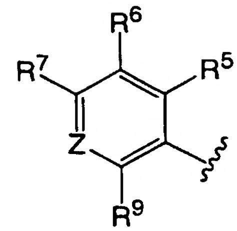
In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

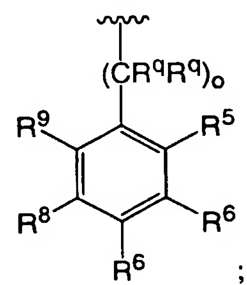
In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m and $-NR^mC_{2-6}$alkylOR^m; or

R^2 is



; or

R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$,

$-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}\text{alkyl}NR^mR^m$, $-OC_{2-6}\text{alkyl}OR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}\text{alkyl}NR^mR^m$, $-NR^mC_{2-6}\text{alkyl}OR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}\text{alkyl}NR^mR^s$, $-OC_{2-6}\text{alkyl}OR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}\text{alkyl}NR^mR^s$, $-NR^mC_{2-6}\text{alkyl}OR^s$ ~~and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo,~~ cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}\text{alkyl}NR^mR^m$, $-OC_{2-6}\text{alkyl}OR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}\text{alkyl}NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}\text{alkyl}NR^mR^s$, $-OC_{2-6}\text{alkyl}OR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}\text{alkyl}NR^mR^s$, $-NR^mC_{2-6}\text{alkyl}OR^s$ and $-NR^mC_{2-6}\text{alkyl}OR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}\text{alkyl}NR^mR^m$, $-O-C_{1-6}\text{alkyl}OR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}\text{alkyl}NR^mR^m$ or $-NR^m-C_{1-6}\text{alkyl}OR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m and $-NR^mC_{2-6}$alkylOR^m;

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$,

$-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

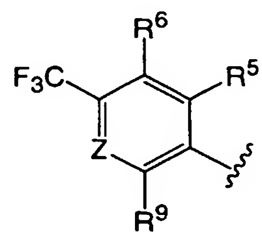
In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, Cl, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$,

$-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

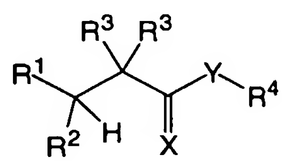
In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$,

$-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

Another aspect of the invention relates to a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

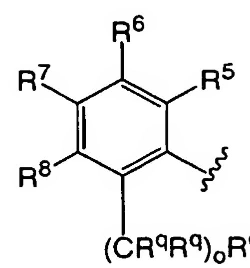
R^3 is H or $C_{1-4}alkyl$;

R^5 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^8 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$,

$-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

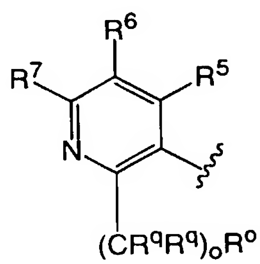
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or

4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(B) R^1 is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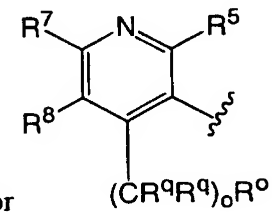


R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$,

$-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, ~~$-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$,~~ $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

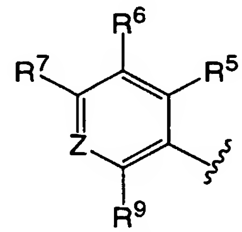
R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2

groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2R^s$, -S(=O)$_2$NR^mR^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^mR^s, -NR^mR^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^mR^s, -N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)$_2R^s$, -N(R^m)S(=O)$_2$NR^mR^s, -NR^mC_{2-6}alkylNR^mR^s, -NR^mC_{2-6}alkylOR^s and -NR^mC_{2-6}alkylOR^m; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is C_{1-8}alkyl, C_{1-5}haloalkyl, I or Br

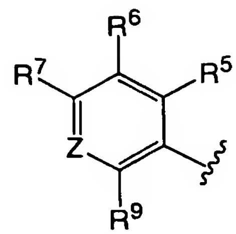
R^9 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m, -NR^m-C_{1-6}alkylOR^m, or -$(CH_2)_nR^c$;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$,

$-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$,

$-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

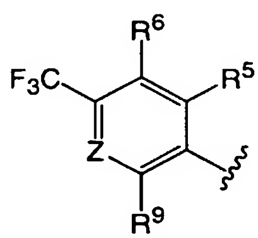
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$,

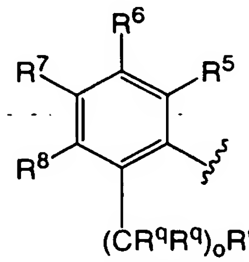
$-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$,

$-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms

selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2R^s$, -S(=O)$_2$NR^mR^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^mR^s, -NR^mR^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^mR^s, -N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)$_2R^s$, -N(R^m)S(=O)$_2$NR^mR^s,

$-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-NR^mR^m$ or $-NR^m-C_{1-4}$haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-5}alkyl, C_{1-4}haloalkyl, I, Br or Cl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

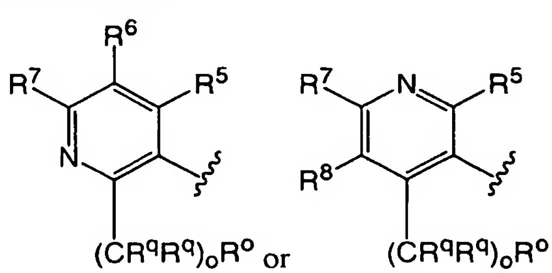
In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$,

$-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; [C_{1-8}alkyl, C_{1-5}haloalkyl, I, Br or Cl]

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$,

$-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, ~~$-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}$~~$alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-NR^mR^m$ or $-NR^m-C_{1-4}$haloalkyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is C_{1-5}alkyl, C_{1-4}haloalkyl, I, Br or Cl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

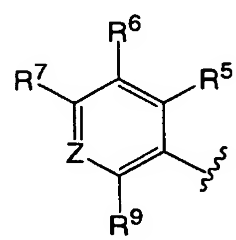
In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is O.

In another embodiment, in conjunction with the novel compound embodiments above and below, Y is NH.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl,

halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a heterocycle selected from indole, 3H-indole, benzo[b]furan, benzothiophene, 1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 1,2,3,4-tetrahydroquinoline, isoquinoline, cinnoline, phthalazine, quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a heterocycle selected from 6-indole, 7-

indole, 6-3H-indole, 7-3H-indole, 6-benzo[b]furan, 7-benzo[b]furan, 6-benzothiophene, 7-benzothiophene, 6-1H-indazole, 7-1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 7-1,2,3,4-tetrahydroquinoline, 8-1,2,3,4-tetrahydroquinoline, isoquinolin-7-yl, isoquinolin-8-yl, 7-cinnoline, 8-cinnoline, phthalazine, 7-quinazoline, 8-quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano,

$-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m.

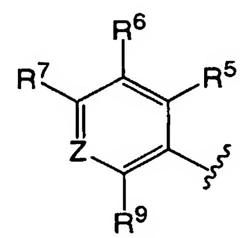
In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

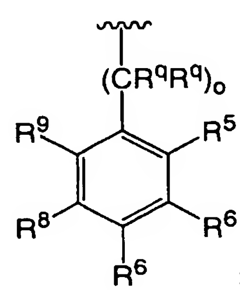
In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m and $-NR^mC_{2-6}$alkylOR^m; or

R^2 is



; or

R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$,

$-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$,

-N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -NR^{m}C$_{2-6}$alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C$_{1-4}$alkyl substituted by 1 or 2 groups selected from C$_{1-2}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and -NR^{m}C$_{2-6}$alkylOR^m.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^2 is -(C(R^q)$_2$)$_o$R^r, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C$_{1-8}$alkyl, C$_{1-4}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m,

$-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

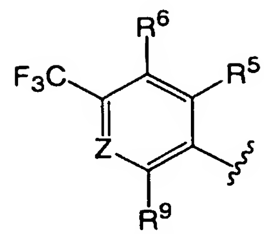
In another embodiment, in conjunction with the novel compound embodiments above and below, R^7 is tert-butyl or trifluoromethyl.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^9 is H.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

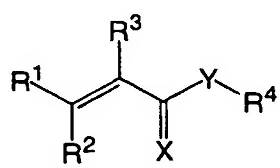
Z is CR^8 or N.

In another embodiment, in conjunction with the novel compound embodiments above and below, R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^n, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$ and -N$R^m$$C_{2-6}$alkylO$R^m$;

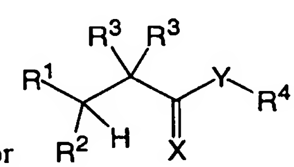
In another embodiment, in conjunction with the novel compound embodiments above and below, Z is CR^8.

In another embodiment, in conjunction with the novel compound embodiments above and below, Z is N.

Another aspect of the invention relates to a method of treating acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, comprising the step of administering a compound having the structure:

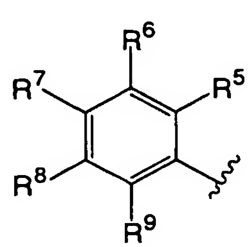


or



wherein:

R^1 is

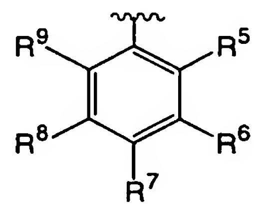


;

or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein

no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

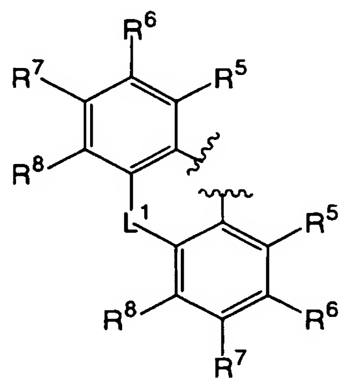
R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},



,

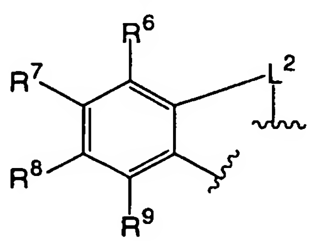
or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

or R^1 and R^2 together are



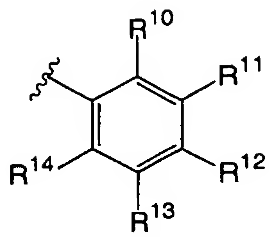
;

R^3 is H or C_{1-4}alkyl; or R^1 and R^3 together are



;

R^4 is



; or

R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl and $-NR^aC(=O)C_{1-6}$alkyl; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O;

R^5 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a or $-NR^a-C_{1-6}$alkylOR^a; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S;

R^6 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a or $-NR^a-C_{1-6}$alkylOR^a; or R^5 and R^6 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the

carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-6}alkyl, (=O), -OC_{1-6}alkyl, -NR^{a}C$_{1-6}$alkyl, -C$_{1-6}$alkylOR^a and C$_{1-6}$alkylNR^{a}R^a, and the available N atoms of the bridge are substituted by R^a, -C$_{1-6}$alkylOR^a or C$_{1-6}$alkylNR^{a}R^a;

R^7 is independently, at each instance, H, C$_{1-9}$alkyl, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OC$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a or -NR^a-C$_{1-6}$alkylOR^a;

R^8 is independently, at each instance, H, C$_{1-9}$alkyl, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OC$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a or -NR^a-C$_{1-6}$alkylOR^a; or R^7 and R^8 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C$_{1-6}$alkyl, (=O), -O-C$_{1-6}$alkyl, -NR^{a}C$_{1-6}$alkyl, -C$_{1-6}$alkylOR^a and C$_{1-6}$alkylNR^{a}R^a, and the available N atoms of the bridge are substituted by R^a, -C$_{1-6}$alkylOR^a or C$_{1-6}$alkylNR^{a}R^a;

R^9 is independently, at each instance, H, C$_{1-9}$alkyl, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OC$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a or -NR^a-C$_{1-6}$alkylOR^a;

R^{10} is independently, at each instance, H, C$_{1-9}$alkyl, -C$_{1-3}$alkylOR^a, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl, -C(=O)OC$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{a}C$_{1-6}$alkyl or -NR^{a}C(=O)C$_{1-6}$alkyl;

R^{11} is independently, at each instance, H, C$_{1-9}$alkyl, -C$_{1-3}$alkylOR^a, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylR^c, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl, -C(=O)OC$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{a}C$_{1-6}$alkyl or -NR^{a}C(=O)C$_{1-6}$alkyl; or R^{10} and R^{11} together are a saturated or unsaturated 3- or

4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$; wherein if R^{10}, R^{12}, R^{13} and R^{14} are all H, then R^{11} is not $-O-C_{1-6}alkylNR^aR^a$ or $-O-C_{1-6}alkylOR^a$;

R^{12} is independently, at each instance, H, $C_{1-9}alkyl$, $-C_{1-3}alkylOR^a$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$; or R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

R^{13} is independently, at each instance, H, $C_{1-9}alkyl$, $-C_{1-3}alkylOR^a$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$,

$-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

R^{14} is independently, at each instance, H, C_{1-9}alkyl, $-C_{1-3}$alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^{a}R^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkylC(=O)OR^a, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^{a}R^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl or $-NR^aC(=O)C_{1-6}$alkyl;

R^a is independently, at each instance, H, phenyl, benzyl or C_{1-6}alkyl;

R^c is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-3}haloalkyl, $-OR^a$ and $-NR^aR^a$; or R^c is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-3}haloalkyl, $-OR^a$ and $-NR^aR^a$;

L^1 is a bond, $-CH_2CH_2-$ or $-CH=CH-$;

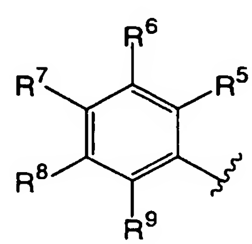
L^2 is NR^a, O, $S(=O)_n$, $-N=CH-$, $-CH_2NR^a-$, $-CH=N-$ or $-NR^aCH_2-$;

X is O, S or NR^a; or X and R^2 together are $=N-CH=CH-$, $=C-O-$, $=C-S-$, or $=C-NR^a-$;

Y is NH or O; and

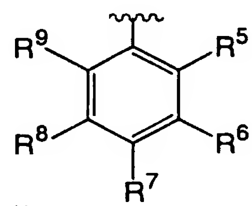
n is independently, at each instance, 0, 1 or 2; with the proviso that when R^1 is 4-chlorophenyl, then R^4 is not 3-methoxyphenyl.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^1 is



or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},



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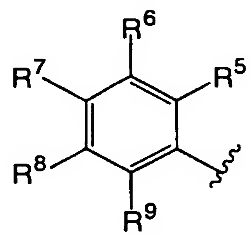
or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7; and

R^3 is H or C_{1-4}alkyl.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^1 is



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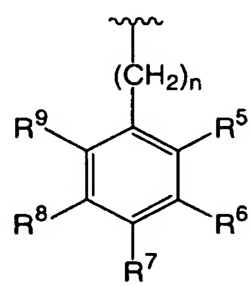
In another embodiment, in conjunction with the method of treatment embodiments above and below, R^7 is independently, at each instance, C_{2-9}alkyl or C_{1-4}haloalkyl.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^1 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the

heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

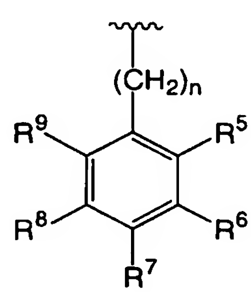
In another embodiment, in conjunction with the method of treatment embodiments above and below, R^2 is



,

or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

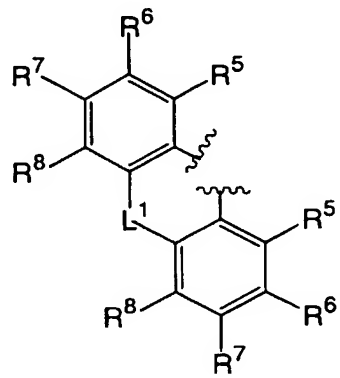
In another embodiment, in conjunction with the method of treatment embodiments above and below, R^2 is



.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^1 and R^2 together are



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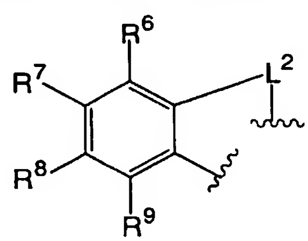
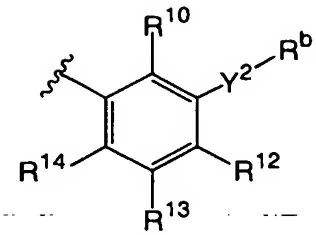
In another embodiment, in conjunction with the method of treatment embodiments above and below, R^1 and R^3 together are



.

In another embodiment, in conjunction with the method of treatment embodiments above and below, X and R^2 together are =N-CH=CH-, =C-O-, =C-S-, or =C-NR^a-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is

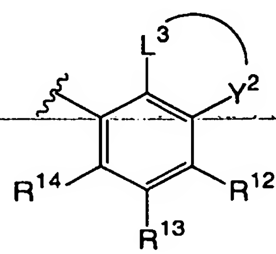


;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^a- or -O-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is



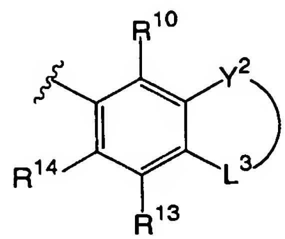
;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0 or 1 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^aR^a, -C_{1-6}alkylNR^aR^a, -C(=O)OR^a, -C(=O)NR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -OC(=O)C_{1-6}alkyl, -NR^aC(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, -C(=O)R^c or -C_{1-3}alkylR^c;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^b- or -O-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is



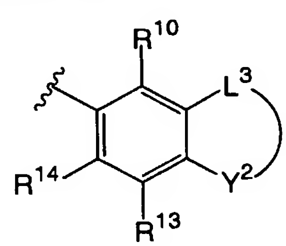
;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl-O-R^a$; and

Y^2 is $-NR^b-$ or -O-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is



;

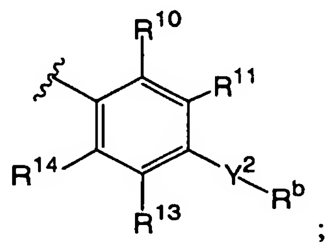
L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$,

$-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl$-O-R^a; and

Y^2 is $-NR^b-$ or -O-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is



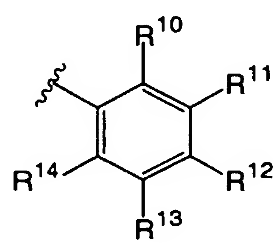
;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl$-O-R^a; and

Y^2 is $-NR^a-$ or -O-.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, $C_{1-6}alkyl$ and $C_{1-3}haloalkyl$; and saturated carbon atoms may be additionally substituted by =O.

In another embodiment, in conjunction with the method of treatment embodiments above and below, R^4 is



;

R^{10} is independently, at each instance, H, $C_{1-9}alkyl$, $-C_{1-3}alkylOR^a$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$;

R^{11} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$R^c$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^a$$C_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl;

C_{1-6}alkylNR^aR^a;

R^{12} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^a$$C_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl;

R^{13} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^a$$C_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl; and

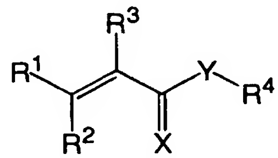
R^{14} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)O$C_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^a$$C_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl; wherein one of R^{10} and R^{12} is not H.

In another embodiment, in conjunction with the method of treatment embodiments above, R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}haloalkyl, -OR^a and -NR^aR^a.

Another aspect of the invention relates to a method of treating acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, comprising the step of administering a compound according to compound description embodiments above--each seperately and alternatively.

Another aspect of the invention involves a method of treating acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis,

bronchial disorders or bladder disorders, comprising the step of administering a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

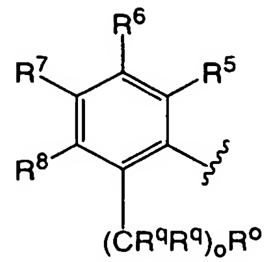
R^3 is H or C_{1-4}alkyl;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

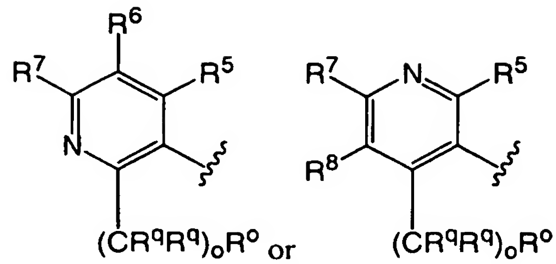
R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

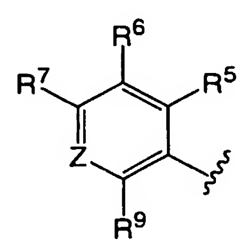
R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl,

benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is C_{1-8}alkyl, C_{1-5}haloalkyl, I or Br

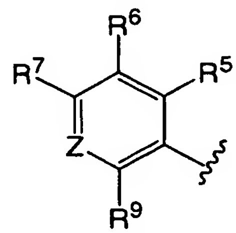
R^9 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$,

$-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$,

$-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2\text{-}6}alkylNR^mR^m$, $-NR^mC_{2\text{-}6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2\text{-}6}alkylNR^mR^s$, $-OC_{2\text{-}6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2\text{-}6}alkylNR^mR^s$, $-NR^mC_{2\text{-}6}alkylOR^s$ and $C_{1\text{-}4}alkyl$ substituted by 1 or 2 groups selected from $C_{1\text{-}2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2\text{-}6}alkylNR^mR^m$, $-OC_{2\text{-}6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2\text{-}6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2\text{-}6}alkylNR^mR^s$, $-OC_{2\text{-}6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2\text{-}6}alkylNR^mR^s$, $-NR^mC_{2\text{-}6}alkylOR^s$ and $-NR^mC_{2\text{-}6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1\text{-}8}alkyl$, $C_{1\text{-}4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2\text{-}6}alkylNR^mR^m$, $-OC_{2\text{-}6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

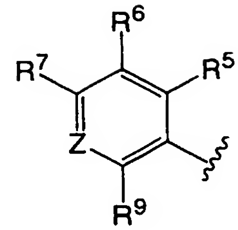
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$,

$-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

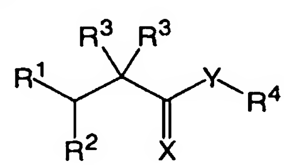
R^7 is C_{2-6}alkyl, C_{1-5}haloalkyl, I or Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

Another aspect of the invention involves a method of treating acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, comprising the step of administering a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

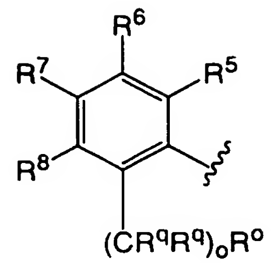
R^3 is H or C_{1-4}alkyl;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

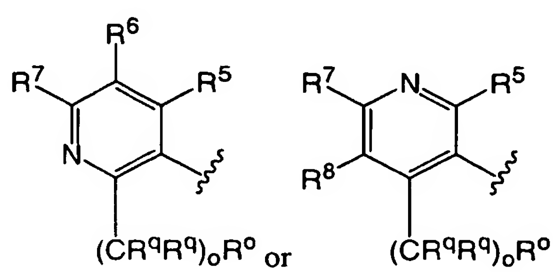
R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$,

$-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

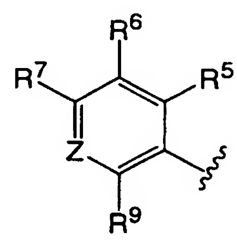
R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-

2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^m, -$S(=O)_nC_{1-6}$alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m, -NR^m-C_{1-6}alkylOR^m, -C(=O)C_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)NR^mC_{1-6}alkyl, -NR^mC(=O)C_{1-6}alkyl -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^mR^s, -NR^mR^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^mR^s, -N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)$_2R^s$, -N(R^m)S(=O)$_2NR^mR^s$, -NR^mC_{2-6}alkylNR^mR^s, -NR^mC_{2-6}alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2NR^mR^m$, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2NR^mR^m$, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^mR^s, -NR^mR^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^mR^s, -N(R^m)C(=NR^m)NR^mR^s, -N(R^m)S(=O)$_2R^s$, -N(R^m)S(=O)$_2NR^mR^s$, -NR^mC_{2-6}alkylNR^mR^s, -NR^mC_{2-6}alkylOR^s and -NR^mC_{2-6}alkylOR^m; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is C_{1-8}alkyl, C_{1-5}haloalkyl, I or Br

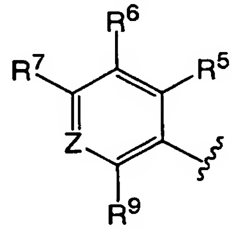
R^9 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{m}R^m, -O-C_{1-6}alkylOR^m, -NR^{m}R^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^{m}R^m, -NR^m-C_{1-6}alkylOR^m, or -(CH$_2$)$_n$R^c;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{m}R^m, -O-C_{1-6}alkylOR^m, -NR^{m}R^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^{m}R^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC_{2-6}alkylNR^{m}R^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^mC_{2-6}alkylNR^{m}R^m or -NR^mC_{2-6}alkylOR^m; or

R^2 is -(C(R^q)$_2$)$_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC_{2-6}alkylNR^{m}R^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^mC_{2-6}alkylNR^{m}R^m, -NR^mC_{2-6}alkylOR^m, -C(=O)R^s, -C(=O)OR^s,

$-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$,

-C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C$_{1-4}$alkyl substituted by 1 or 2 groups selected from C$_{1-2}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and -NR^{m}C$_{2-6}$alkylOR^m;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C$_{1-8}$alkyl, C$_{1-4}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n,

$-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

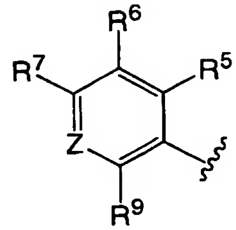
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^7 is C_{2-6}alkyl, C_{1-5}haloalkyl, I or Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

~~Z is CR^8 or N.~~

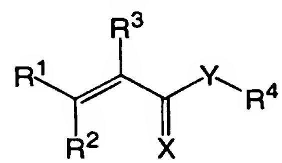
Another aspect of the invention involves a pharmaceutical composition comprising a compound according to any of the above embodiments and a pharmaceutically-acceptable diluent or carrier.

Another aspect of the invention involves the use of any of the above compound embodiments as a medicament.

Another aspect of the invention relates to the use of a compound according the any one of the above embodiments in the manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration,

duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders.

Another aspect of the invention relates to the manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, wherein the medicament contains a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$,

$-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

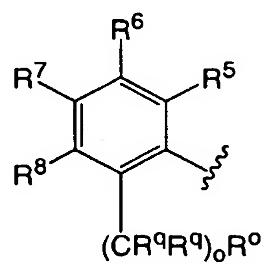
R^3 is H or $C_{1-4}alkyl$;

R^5 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^8 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

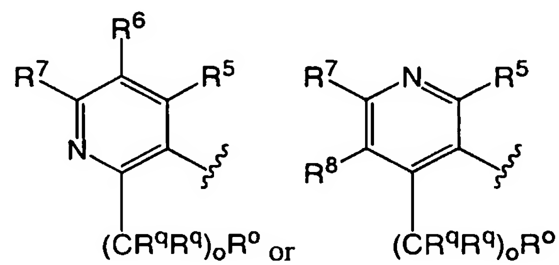
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or

2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$,

$-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

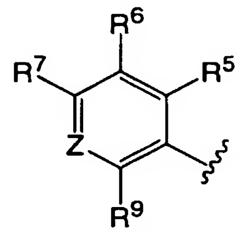
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

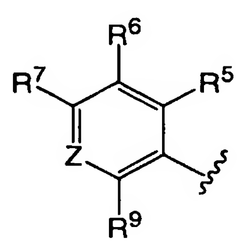
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from

C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$,

$-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

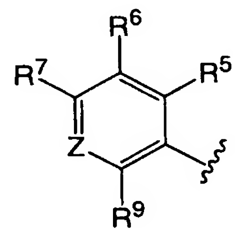
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$,

$-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^7 is C_{2-6}alkyl, C_{1-5}haloalkyl, I or Br;

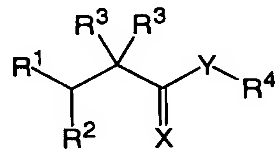
R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

Another aspect of the invention relates to the manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints

with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, wherein the medicament contains a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

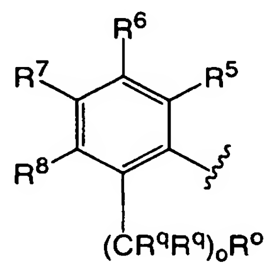
R^3 is H or C_{1-4}alkyl;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m, -NR^m-C_{1-6}alkylOR^m, or -$(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m; and

(A) R^1 is



R^2 is H, -OR^m, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$,

$-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

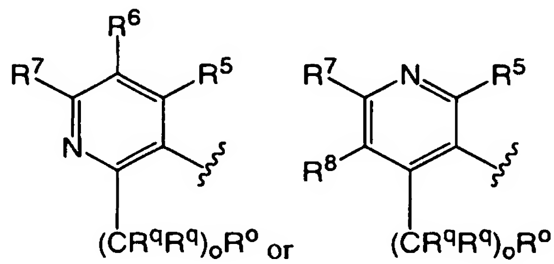
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$,

$-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo,

cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

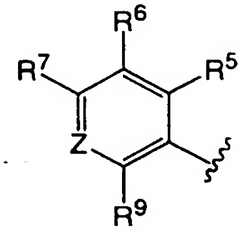
R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

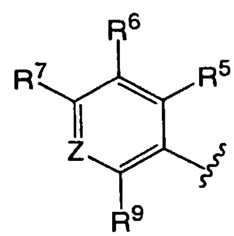
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S,

wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected

from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

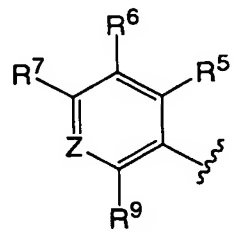
R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, -OR^m, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^n, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2NR^mR^m$, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2NR^mR^m$, -$NR^m$$C_{2-6}$alkyl$NR^mR^m$, -$NR^m$$C_{2-6}$alkyl$OR^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)$NR^mR^s$, -C(=$NR^m$)$NR^mR^s$, -$OR^s$, -OC(=O)$R^s$, -OC(=O)$NR^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkyl$NR^mR^s$, -O$C_{2-6}$alkyl$OR^s$, -$SR^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)$NR^mR^s$, -$NR^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)$NR^mR^s$, -N($R^m$)C(=$NR^m$)$NR^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -$NR^m$$C_{2-6}$alkyl$NR^mR^s$, -$NR^m$$C_{2-6}$alkyl$OR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m,

$-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^7 is C_{2-6}alkyl, C_{1-5}haloalkyl, I or Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

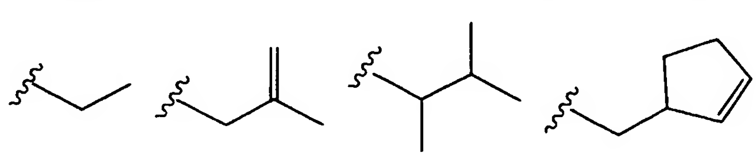
Y is NH; and

Z is CR^8 or N.

The compounds of this invention may have in general several asymmetric centers and are typically depicted in the form of racemic mixtures. This invention is intended to encompass racemic mixtures, partially racemic mixtures and separate enantiomers and diasteromers.

Unless otherwise specified, the following definitions apply to terms found in the specification and claims:

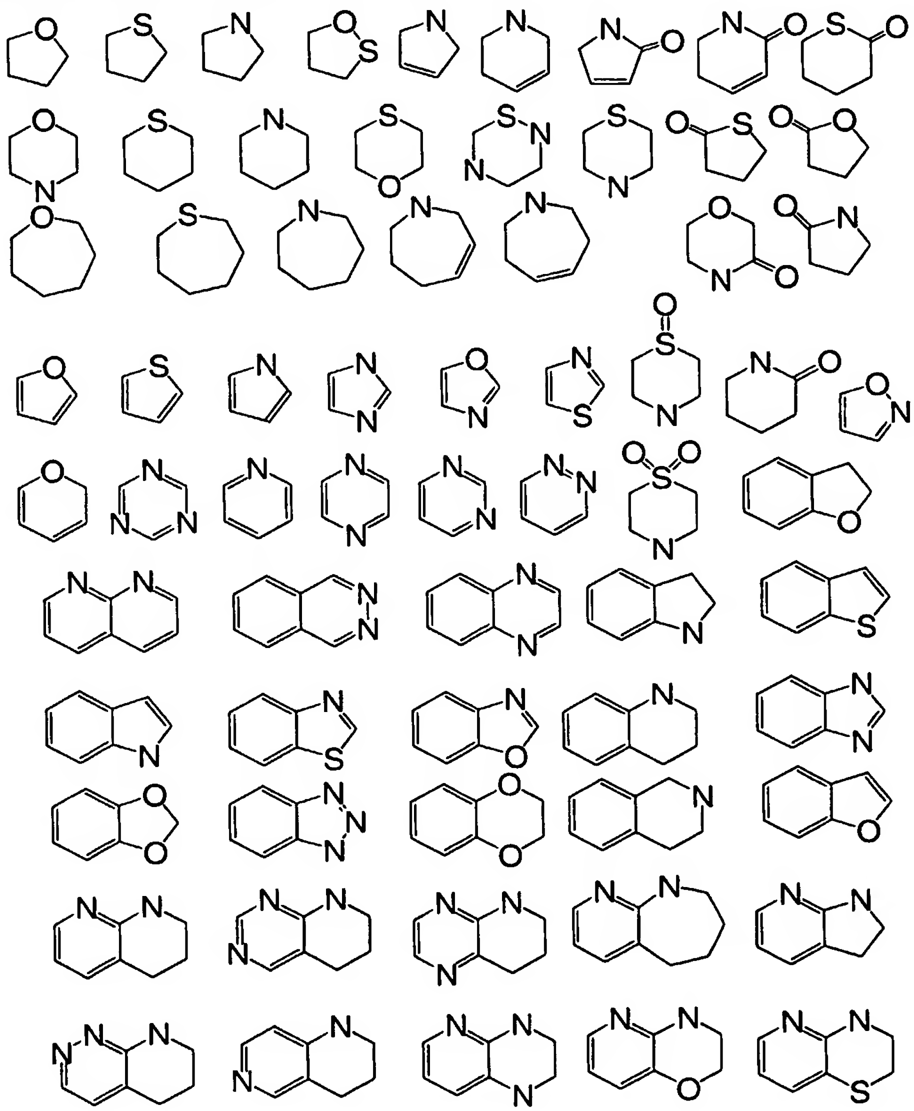
"$C_{\alpha-\beta}$alkyl" means an alkyl group comprising from α to β carbon atoms in a branched, cyclical or linear relationship or any combination of the three. The alkyl groups described in this section may also contain a double or triple bond. Examples of C_{1-6}alkyl include, but are not limited to the following:

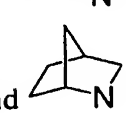


"Halo" means a halogen atoms selected from F, Cl, Br and I.

"$C_{\alpha-\beta}$haloalkyl" means an alkyl group, as described above, wherein any number--at least one--of the hydrogen atoms attached to the alkyl chain are replaced by F, Cl, Br or I.

"Heterocycle" means a ring comprising at least one carbon atom and at least one other atom selected from N, O and S. Examples of heterocycles that may be found in the claims include, but are not limited to, the following:



and .

"Pharmaceutically-acceptable salt" means a salt prepared by conventional means, and are well known by those skilled in the art. The "pharmacologically acceptable salts" include basic salts of inorganic and organic acids, including but not limited to hydrochloric acid, hydrobromic acid, sulfuric acid, phosphoric acid, methanesulphonic acid, ethanesulfonic acid, malic acid, acetic acid, oxalic acid, tartaric acid, citric acid, lactic acid, fumaric acid, succinic acid, maleic acid, salicylic acid, benzoic acid, phenylacetic acid, mandelic acid and the like. When compounds of the invention include an acidic function such as a carboxy group, then suitable pharmaceutically acceptable cation pairs for the carboxy group are well known to those skilled in the art and include alkaline, alkaline earth, ammonium, quaternary ammonium cations and the like. For additional examples of "pharmacologically acceptable salts," *see infra* and Berge et al., J. Pharm. Sci. 66:1 (1977).

"Leaving group" generally refers to groups readily displaceable by a nucleophile, such as an amine, a thiol or an alcohol nucleophile. Such leaving groups are well known in the art. Examples of such leaving groups include, but are not limited to, N-hydroxysuccinimide, N-hydroxybenzotriazole, halides, triflates, tosylates and the like. Preferred leaving groups are indicated herein where appropriate.

"Protecting group" generally refers to groups well known in the art which are used to prevent selected reactive groups, such as carboxy, amino, hydroxy, mercapto and the like, from undergoing undesired reactions, such as nucleophilic, electrophilic, oxidation, reduction and the like. Preferred protecting groups are indicated herein where appropriate. Examples of amino protecting groups include, but are not limited to, aralkyl, substituted aralkyl, cycloalkenylalkyl and substituted cycloalkenyl alkyl, allyl, substituted allyl, acyl, alkoxycarbonyl, aralkoxycarbonyl, silyl and the like. Examples of aralkyl include, but are not limited to, benzyl, ortho-methylbenzyl, trityl and benzhydryl, which can be optionally substituted with halogen, alkyl, alkoxy, hydroxy, nitro, acylamino, acyl and the like, and salts, such as phosphonium and ammonium salts. Examples of aryl groups include phenyl, naphthyl, indanyl, anthracenyl, 9-(9-phenylfluorenyl), phenanthrenyl, durenyl and the like. Examples of cycloalkenylalkyl or substituted cycloalkylenylalkyl radicals, preferably have 6-10 carbon atoms, include, but are not limited to, cyclohexenyl

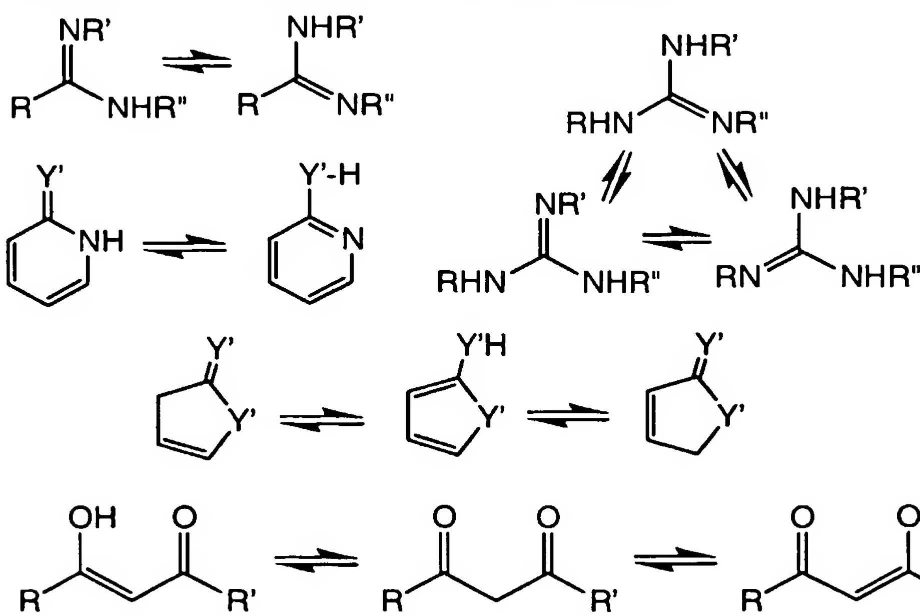
methyl and the like. Suitable acyl, alkoxycarbonyl and aralkoxycarbonyl groups include benzyloxycarbonyl, t-butoxycarbonyl, iso-butoxycarbonyl, benzoyl, substituted benzoyl, butyryl, acetyl, tri-fluoroacetyl, tri-chloro acetyl, phthaloyl and the like. A mixture of protecting groups can be used to protect the same amino group, such as a primary amino group can be protected by both an aralkyl group and an aralkoxycarbonyl group. Amino protecting groups can also form a heterocyclic ring with the nitrogen to which they are attached, for example, 1,2-bis(methylene)benzene, phthalimidyl, succinimidyl, maleimidyl and the like and where these heterocyclic groups can further include adjoining aryl and cycloalkyl rings. In addition, the heterocyclic groups can be mono-, di- or tri-substituted, such as nitrophthalimidyl. Amino groups may also be protected against undesired reactions, such as oxidation, through the formation of an addition salt, such as hydrochloride, toluenesulfonic acid, trifluoroacetic acid and the like. Many of the amino protecting groups are also suitable for protecting carboxy, hydroxy and mercapto groups. For example, aralkyl groups. Alkyl groups are also suitable groups for protecting hydroxy and mercapto groups, such as *tert*-butyl.

Silyl protecting groups are silicon atoms optionally substituted by one or more alkyl, aryl and aralkyl groups. Suitable silyl protecting groups include, but are not limited to, trimethylsilyl, triethylsilyl, tri-isopropylsilyl, *tert*-butyldimethylsilyl, dimethylphenylsilyl, 1,2-bis(dimethylsilyl)benzene, 1,2-bis(dimethylsilyl)ethane and diphenylmethylsilyl. Silylation of an amino groups provide mono- or di-silylamino groups. Silylation of aminoalcohol compounds can lead to a N,N,O-tri-silyl derivative. Removal of the silyl function from a silyl ether function is readily accomplished by treatment with, for example, a metal hydroxide or ammonium fluoride reagent, either as a discrete reaction step or in situ during a reaction with the alcohol group. Suitable silylating agents are, for example, trimethylsilyl chloride, *tert*-butyl-dimethylsilyl chloride, phenyldimethylsilyl chloride, diphenylmethyl silyl chloride or their combination products with imidazole or DMF. Methods for silylation of amines and removal of silyl protecting groups are well known to those skilled in the art. Methods of preparation of these amine derivatives from corresponding amino acids, amino acid amides or amino acid esters are also well known to those skilled

in the art of organic chemistry including amino acid/amino acid ester or aminoalcohol chemistry.

Protecting groups are removed under conditions which will not affect the remaining portion of the molecule. These methods are well known in the art and include acid hydrolysis, hydrogenolysis and the like. A preferred method involves removal of a protecting group, such as removal of a benzyloxycarbonyl group by hydrogenolysis utilizing palladium on carbon in a suitable solvent system such as an alcohol, acetic acid, and the like or mixtures thereof. A t-butoxycarbonyl protecting group can be removed utilizing an inorganic or organic acid, such as HCl or trifluoroacetic acid, in a suitable solvent system, such as dioxane or methylene chloride. The resulting amino salt can readily be neutralized to yield the free amine. Carboxy protecting group, such as methyl, ethyl, benzyl, *tert*-butyl, 4-methoxyphenylmethyl and the like, can be removed under hydroylsis and hydrogenolysis conditions well known to those skilled in the art.

It should be noted that compounds of the invention may contain groups that may exist in tautomeric forms, such as cyclic and acyclic amidine and guanidine groups, heteroatom substituted heteroaryl groups (Y' = O, S, NR), and the like, which are illustrated in the following examples:



and though one form is named, described, displayed and/or claimed herein, all the tautomeric forms are intended to be inherently included in such name, description, display and/or claim.

Prodrugs of the compounds of this invention are also contemplated by this invention. A prodrug is an active or inactive compound that is modified chemically through in vivo physiological action, such as hydrolysis, metabolism and the like, into a compound of this invention following administration of the prodrug to a patient. The suitability and techniques involved in making and using prodrugs are well known by those skilled in the art. For a general discussion of prodrugs involving esters see Svensson and Tunek Drug Metabolism Reviews 165 (1988) and Bundgaard Design of Prodrugs, Elsevier (1985). Examples of a masked carboxylate anion include a variety of esters, such as alkyl (for example, methyl, ethyl), cycloalkyl (for example, cyclohexyl), aralkyl (for example, benzyl, p-methoxybenzyl), and alkylcarbonyloxyalkyl (for example, pivaloyloxymethyl). Amines have been masked as arylcarbonyloxymethyl substituted derivatives which are cleaved by esterases in vivo releasing the free drug and formaldehyde (Bungaard J. Med. Chem. 2503 (1989)). Also, drugs containing an acidic NH group, such as imidazole, imide, indole and the like, have been masked with N-acyloxymethyl groups (Bundgaard Design of Prodrugs, Elsevier (1985)). Hydroxy groups have been masked as esters and ethers. EP 039,051 (Sloan and Little, 4/11/81) discloses Mannich-base hydroxamic acid prodrugs, their preparation and use.

Experimental

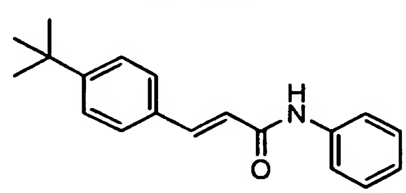
General

Unless otherwise noted, all materials were obtained from commercial suppliers and used without further purification. All parts are by weight and temperatures are in Degrees centigrade unless otherwise indicated. All compounds showed NMR spectra consistent with their assigned structures. Melting points were determined on a Buchi apparatus and are uncorrected. Mass spectral data was determined by electrospray ionization technique. All examples were purified to >95% purity as determined by high-performance liquid chromatography (HPLC). Unless otherwise stated, reactions were run at room temperature.

The following abbreviations are used:

aq. -	aqueous
cond -	concentrated
DMF -	*N,N*-dimethylformamide
Et_2O -	diethyl ether
EtOAc -	ethyl acetate
EtOH -	ethyl alcohol
h -	hour
min -	minutes
MeOH -	methyl alcohol
satd -	saturated
THF –	tetrahydrofuran

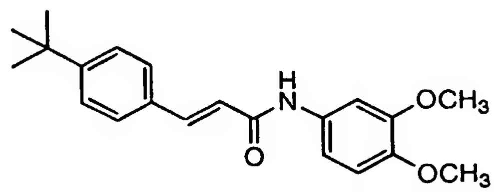
Example 1



(2E)-3-[4-(tert-Butyl)phenyl]-N-phenylprop-2-enamide. To a 10 mL glass vial was added 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 0.98 mmol, EMKA-Chemie) followed by CH_2Cl_2 (5 mL), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (225 mg, 1.17 mmol, Bachem) and aniline (98 uL, 100 mg,

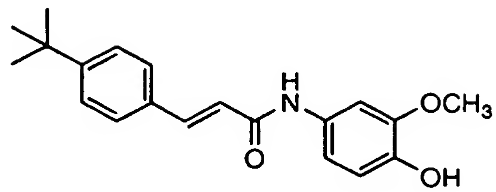
1.08 mmol, Aldrich). The reaction mixture was magnetically stirred at 25 °C for 24 h. EtOAc was added (60 mL) and the mixture washed successively with 1 N NaOH (2 x 20 mL), 1 N HCl (20 mL), water (20 mL) and satd NaCl (20 mL), dried over $MgSO_4$, filtered and concentrated. Recrystallization from hexane and CH_2Cl_2 provided the title product as white crystals. MP 141 °C. MS (ESI, pos. ion) *m/z*: 280 (M+1).

Example 2

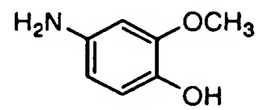


(2E)-N-(3,4-Dimethoxyphenyl)-3-[4-(tert-butyl)phenyl]prop-2-enamide. To a 20 mL round-bottomed flask equipped with reflux condenser and drying tube was added 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 0.98 mmol, EMKA-Chemie) followed by CH_2Cl_2 (5 mL), oxalyl chloride (90 uL, 130 mg, 1.03 mmol, Aldrich) and DMF (1 uL). The reaction mixture was magnetically stirred and heated at reflux for 30 min. The reaction mixture was concentrated in vacuo and the residue dissolved in acetone (2 mL). The solution was added to a mixture of 3,4-dimethoxyaniline (180 mg, 1.17 mmol, Aldrich), potassium carbonate (200 mg), water (2 mL) and acetone (2 mL), magnetically stirred at 25 °C in a 10 mL glass vial. The reaction mixture was stirred at 25 °C for 16 h then diluted with EtOAc (60 mL) and washed successively with 1 N HCl (20 mL), 1 N NaOH (20 mL), water (20 mL) and satd NaCl (20 mL), dried over $MgSO_4$, filtered and concentrated. Recrystallization from hexane and CH_2Cl_2 provided the title product as a yellow solid. MP 115-116 °C. MS (ESI, pos. ion) *m/z*: 340 (M+1).

Example 3



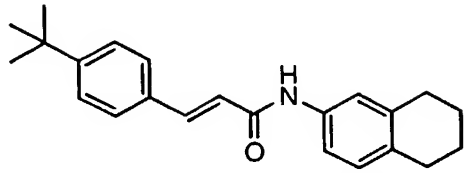
(2E)-3-[4-(tert-Butyl)phenyl]-N-(4-hydroxy-3-methoxyphenyl)prop-2-enamide.



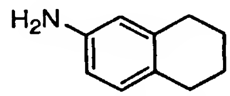
(a). 4-Amino-2-methoxyphenol. To a round-bottomed flask was added 4-nitroguaiacol (500 mg, 3.0 mmol, Aldrich) and anhydrous EtOH (50 mL). The solution was stirred magnetically under N_2 and treated with 10% Pd on carbon (200 mg, Aldrich). The suspension was purged with H_2 and then stirred at 25 °C under 1 atm H_2 for 16 h. The suspension was purged with N_2, filtered through Celite and concentrated in vacuo to provide a dark solid. The solid was washed with 1:1 CH_2Cl_2:hexane and dried in vacuo to provide the title product as pale brown crystals. MS (ESI, pos. ion) *m/z*: 140 (M+1).

(b). (2E)-3-[4-(tert-Butyl)phenyl]-N-(4-hydroxy-3-methoxyphenyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 2**, 4-amino-2-methoxyphenol, **Example 3(a)**, (164 mg, 1.18 mmol) and 4-*t*-butyl-*trans*-cinnamic acid (200 mg, 0.98 mmol, EMKA-Chemie) provided, after recrystallization of the crude product from CH_2Cl_2 and hexane, the title product as brown crystals. MP 203-204 °C. MS (ESI, pos. ion) *m/z*: 326 (M+1).

Example 4



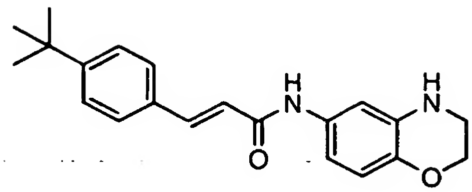
(2E)-3-[4-(tert-Butyl)phenyl]-N-(2-5,6,7,8-tetrahydronaphthyl)prop-2-enamide.



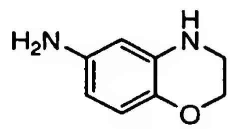
(a). 2-5,6,7,8-Tetrahydronaphthylamine. To a round-bottomed flask was added 6-amino-1,2,3,4-tetrahydronaphthalene (500 mg, 3.10 mmol, Maybridge), triethylsilane (2.50 mL, 15.5 mmol, Aldrich) and trifluoroacetic acid (5.0 mL, 66 mmol, Aldrich). The reaction mixture was magnetically stirred vigorously, at 25 °C, for 2 h. The solvents were removed in vacuo and the residue dissolved in EtOAc (50 mL) and extracted with 1 N HCl (100 mL, then 50 mL). The combined aqueous acidic extract was washed with EtOAc (50 mL) then basified with 5 N NaOH, at 0 °C, to pH 10. The mixture was extracted with CH_2Cl_2 (3 x 50 mL), the combined organic extract washed with water (50 mL), satd NaCl (50 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide the title product as a brown oil. MS (ESI, pos. ion) *m/z*: 148 (M+1).

(b). (2E)-3-[4-(tert-Butyl)phenyl]-N-(2-5,6,7,8-tetrahydronaphthyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 2,** 2-5,6,7,8-tetrahydronaphthylamine, **Example 4(a),** (173 mg, 1.18 mmol) and 4-*t*-butyl-*trans*-cinnamic acid (200 mg, 0.98 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (4:1 hexane:EtOAc) followed by re-crystallization from CH_2Cl_2 and hexane, the title product as white crystals. MP 198-199 °C. MS (ESI, pos. ion) *m/z*: 334 (M+1).

Example 5



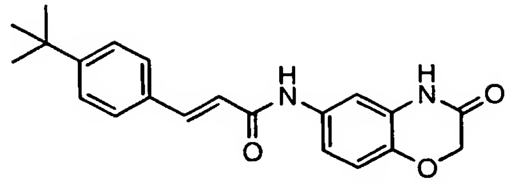
(2E)-N-(2H,3H,4H-Benzo[3,4-e]1,4-oxazaperhydroin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide.



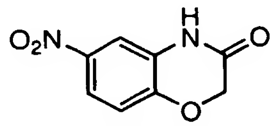
(a) 2H,3H,4H-Benzo[e]1,4-oxazaperhydroine-6-ylamine. To a round-bottomed flask was added 2-amino-4-nitrophenol (1.0 g, 6.5 mmol, Aldrich), potassium carbonate (1.8 g, 13 mmol), DMF (5 mL) and 1,2-dibromoethane (0.59 mL, 6.9 mmol, Aldrich). The mixture was magnetically stirred and heated in a 125 °C oil bath, under N_2, for 2.5 h. After allowing to cool to 25 °C, the reaction mixture was diluted with EtOAc (100 mL), washed with 1 N NaOH (3 x 50 mL), water (50 mL), satd NaCl (50 mL), dried over Na_2SO_4, filtered and concentrated to provide a dark residue [MS (ESI, pos. ion) *m/z*: 181 (M+1)]. The crude product was dissolved in EtOH (100 mL), the solution was purged with N_2, treated with 10% Pd on carbon (450 mg, Aldrich), purged with H_2 then magnetically stirred under 1 atm H_2 for 2 h. After purging again with N_2, the suspension was filtered through Celite and concentrated in vacuo. Purification by silica gel chromatography (95:5 CH_2Cl_2: 2 M NH_3 in EtOH) provided the title product as a viscous brown oil. MS (ESI, pos. ion) *m/z*: 151 (M+1).

(b) (2E)-N-(2H,3H,4H-Benzo[3,4-e]1,4-oxazaperhydroin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 2**, 2H,3H,4H-benzo[e]1,4-oxazaperhydroine-6-ylamine, **Example 5(a)**, (176 mg, 1.18 mmol) and 4-*t*-butyl-*trans*-cinnamic acid (200 mg, 0.98 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (step gradient, 6:3:1 CH_2Cl_2:hexane:EtOAc then 9:1 hexane:EtOAc) the title product as a yellow solid. MP 108-114 °C. MS (ESI, pos. ion) *m/z*: 337 (M+1).

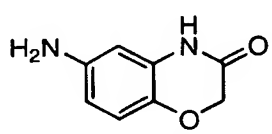
Example 6



(2E)-3-[4-(tert-Butyl)phenyl]-N-(3-oxo(2H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide.



(a) 6-Nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. A mixture of 4-nitro-2-aminophenol (4.6 g, 30 mmol, Aldrich), benzyltrimethylammonium chloride (6.8 g, 30 mmol, Aldrich) and solid $NaHCO_3$ (12.6 g, 150 mmol) in chloroform (100 mL) was magnetically stirred at 0 °C in a round-bottomed flask and treated dropwise with chloroacetyl chloride (2.9 mL, 33 mmol, Aldrich) over a period of 30 min. After the addition was complete, the reaction mixture was stirred at 0 °C for 1 h, then at 50 °C overnight. The solvent was removed in vacuo and the residue treated with water (50 mL), collected by filtration and washed with water. The solid was recrystallized from EtOH to provide 6-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. MS (ESI, neg. ion) *m/z*: 193 (M-1).

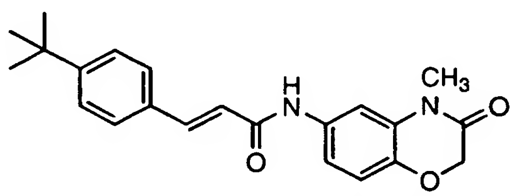


(b) 6-Amino-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. To a suspension of 6-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 6(a),** (0.50 g, 2.6 mmol) and CuCl (0.77 g, 7.8 mmol, Aldrich) in anhydrous MeOH (25 mL), magnetically stirred at 25 °C in a round-bottomed flask, was added potassium borohydride (0.98 g, 18 mmol, Aldrich) in portions. The reaction mixture was stirred at 25 °C for 0.5 h, then the solvent was removed in vacuo and the residue suspended in water (30 mL) and extracted with EtOAc (5 x 20 mL). The combined organic extracts were washed with satd NaCl, dried over Na_2SO_4,

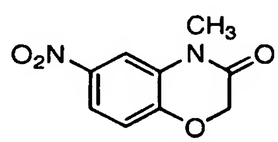
filtered and concentrated in vacuo to provide the title product as a brown solid. MS (ESI, pos. ion) *m/z*: 165 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(3-oxo(2H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 6-amino-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 6(b)**, (207 mg, 1.26 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (258 mg, 1.26 mmol EMKA-Chemie) provided, after recrystallization from EtOAc and hexane, the title compound as a pale yellow solid. MP > 280 °C. MS (ESI, pos. ion) *m/z*: 351 (M+1).

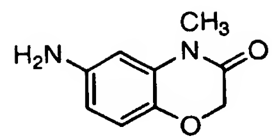
Example 7



(2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide.



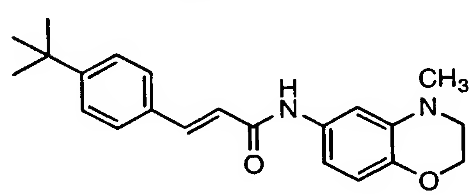
(a) 4-Methyl-6-nitro-2H-benzo[e]1,4-oxazaperhydroin-3-one. A mixture of 6-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 6(a)**, (970 mg, 25 mmol), benzyltrimethylammonium chloride (114 mg, 0.50 mmol, Aldrich) and iodomethane (0.47 mL, 7.5 mmol, Aldrich) in CH_2Cl_2 (20 mL) was stirred magnetically in a 100 mL round-bottomed flask and treated with CsOH monohydrate (4.2 g, 25 mmol, Aldrich). The reaction mixture was stirred at 25 °C for 1 h, treated with water (5 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic extract was washed with water (5 mL), satd NaCl (5 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The residue was purified by silica gel chromatography (9:1 hexane:EtOAc) to provide the title product. MS (ESI, pos. ion) *m/z*: 209 (M+1).



(b) 6-Amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one. To a solution of 4-methyl-6-nitro-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 7(a),** (700 mg, 3.4 mmol) and $NiCl_2 \cdot 6H_2O$ (400 mg, 1.7 mmol, Aldrich) in MeOH (10 mL), magnetically stirred in a 100 mL round-bottomed flask at 25 °C, was added $NaBH_4$ (190 mg, 5.1 mmol, Aldrich) in portions. The reaction mixture was stirred for 30 min then concentrated in vacuo. Purification by silica gel chromatography (CH_2Cl_2/EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 179 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and 6-amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 7(b),** (180 mg, 1.0 mmol) provided, after purification by silica gel chromatography (4:1 CH_2Cl_2:EtOAc), the title product as a pale yellow solid. MP 201–203 °C. MS (ESI, pos. ion) *m/z*: 365 (M+1).

Example 8

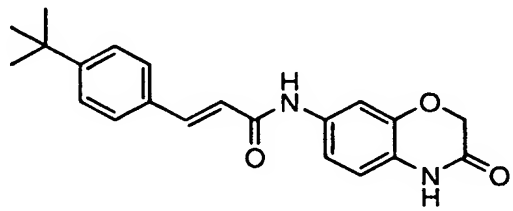


(2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl(2H,3H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide.

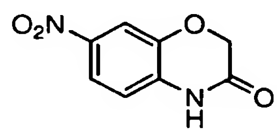
To a solution of lithium aluminum hydride (2.0 mL, 2.0 mmol, 1.0 M in THF, Aldrich), magnetically stirred at 0 °C in a round-bottomed flask under N_2, was added 6-amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 7b,** (180 mg, 1.0 mmol). The reaction mixture was allowed to warm to 25 °C and stirred at that temperature for 1 h. The reaction was quenched by the dropwise addition of 20% H_2O/THF (1.2 mL), followed by 5 N NaOH (0.2 mL). The mixture was stirred at 25 °C for 30 min, then filtered and washed with EtOAc.

The filtrate was dried over Na_2SO_4, filtered and concentrated in vacuo [MS (ESI, pos. ion) *m/z*: 165 (M+1)]. Analogous to the procedure used to prepare **Example 1**, the crude product and 4-*tert*-butyl-*trans*-cinnamic acid provided the title compound as a pale yellow solid. MP 186–188 °C. MS (ESI, pos. ion) *m/z*: 351 (M+1).

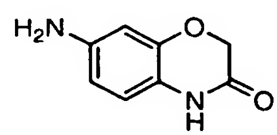
Example 9



(2E)-3-[4-(tert-Butyl)phenyl]-N-(3-oxo(2H,4H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide.



(a) 7-Nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. Analogous to the procedure used for the preparation of 6-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 6(a),** 5-nitro-2-aminophenol (4.6 g, 30 mmol, Aldrich) and chloroacetyl chloride (2.9 mL, 33 mmol, Aldrich) provided, after recrystallization from EtOH, 7-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. MS (ESI, neg. ion) *m/z*: 193 (M−1).

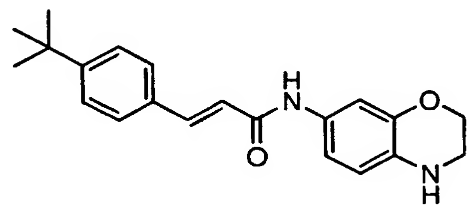


(b) 7-Amino-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one. A mixture of 7-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 9(a)**, (970 mg, 5.0 mmol) and 10% Pd on carbon (100 mg, Aldrich) in MeOH (20 mL) was magnetically stirred in a round-bottomed flask under 1 atm H_2 for 2 h. The mixture was purged with N_2 and filtered through a pad of Celite. Concentration in vacuo provided the title product. MS (ESI, pos. ion) *m/z*: 165 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(3-oxo(2H,4H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide. Analogous to the procedure used to

prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and 7-amino-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 9(b),** (164 mg, 1.0 mmol) provided, after purification by silica gel chromatography (4:1 CH_2Cl_2:EtOAc), the title product as a pale yellow solid. MP 226–227 °C. MS (ESI, pos. ion) *m/z*: 351 (M+1).

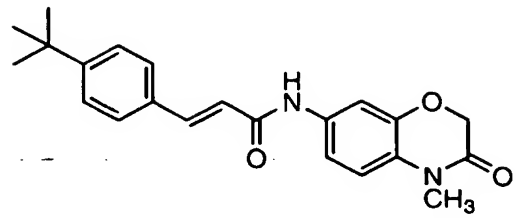
Example 10



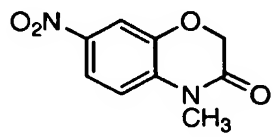
(2E)-N-(2H,3H,4H-Benzo[e]1,4-oxazaperhydroin-7-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide.

To a solution of borane-THF complex (2.5 mL, 2.5 mmol ,1.0 M in THF, Aldrich), magnetically stirred at 0 °C under N_2 in a round-bottomed flask equipped with a reflux condenser, was added 7-amino-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 9(b),** (160 mg, 1.0 mmol). The reaction mixture was stirred at reflux for 2 h, then treated with EtOH (0.5 mL) and reflux continued for an additional 1 h. The mixture was treated with cond HCl (0.5 mL) and reflux continued for an additional 1 h. The solvent was removed in vacuo and the residue treated with 1 N NaOH (5 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic extracts were washed with satd NaCl, dried over Na_2SO_4, filtered and concentrated in vacuo to provide the crude aniline [MS (ESI, pos. ion) *m/z*: 151 (M+1)]. Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and the crude aniline, after purification by silica gel chromatography (85:15 CH_2Cl_2:EtOAc), provided the title product as a pale yellow solid. MP 186–188 °C. MS (ESI, pos. ion) *m/z*: 337 (M+1).

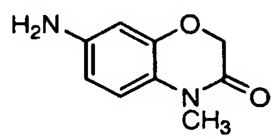
Example 11



(2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide.



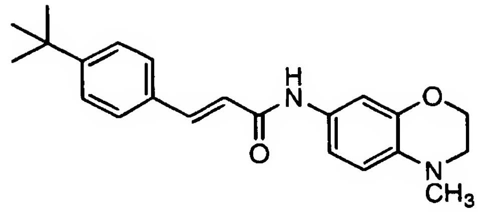
(a) 4-Methyl-7-nitro-2H-benzo[e]1,4-oxazaperhydroin-3-one. Analogous to the procedure used to prepare **Example 7(a),** 7-nitro-2H,4H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 9(a)**, (970 mg, 25 mmol), benzyltrimethylammonium chloride (110 mg, 0.50 mmol, Aldrich), iodomethane (0.47 mL, 7.5 mmol, Aldrich) and CsOH hydrate (4.2 g, 25 mmol, Aldrich), after purification by silica gel chromatography (9:1 hexane:EtOAc), provided the title product. MS (ESI, neg. ion) *m/z*: 207 (M−1).



(b) 7-Amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one. Analogous to the procedure used to prepare **Example 3(a)**, 4-methyl-7-nitro-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 11(a)**, (1.0 g, 5.0 mmol) provided, after recrystallization from EtOH, the title product. MS (ESI, pos. ion) *m/z*: 179 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and 7-amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 11b**, (164 mg, 1.0 mmol) provided, after purification by silica gel chromatography (85:15 CH_2Cl_2:EtOAc), the title product as a pale yellow solid. MP 194–195 °C. MS (ESI, pos. ion) *m/z*: 365 (M+1).

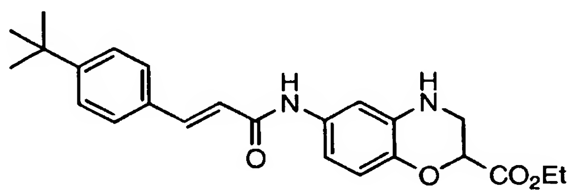
Example 12



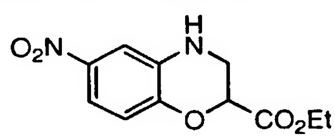
(2E)-3-[4-(tert-Butyl)phenyl]-N-(4-methyl(2H,3H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide.

Analogous to the procedure used for the preparation of **Example 10,** 7-amino-4-methyl-2H-benzo[e]1,4-oxazaperhydroin-3-one, **Example 11(b),** (180 mg, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (85:15 CH_2Cl_2:EtOAc), the title product as a pale yellow solid. MP 232–233 °C. MS (ESI, pos. ion) *m/z*: 351 (M+1).

Example 13

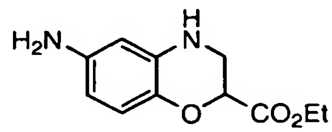


Ethyl 6-{(2E)-3-[4-(tert-butyl)phenyl]prop-2-enoylamino}-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate.



(a) Ethyl 6-nitro-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate. A solution of ethyl 2,3-dibromopropionate (4.8 mL, 33 mmol, Aldrich) in acetone (10 mL, Aldrich) was added to a mixture of 2-amino-4-nitrophenol (4.6 g, 30 mmol, Aldrich) in 80 mL of acetone in a 150 mL round-bottomed flask at 25 °C. After the addition, the mixture was stirred at 60 °C for 48 h. The solvent was removed in vacuo, and the residue was treated with water (30 mL) and extracted with CH_2Cl_2 (3 x 50 mL). The combined organic phases were washed with satd NaCl (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The

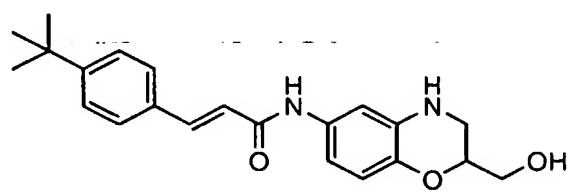
residue was purified by silica gel chromatography (9:1 CH_2Cl_2:EtOAc) to give the title product. MS (ESI, pos. ion) *m/z*: 253 (M+1).



(b) Ethyl 6-amino-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate. Analogous to the procedure used to prepare **Example 3(a)**, ethyl 6-nitro-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate, **Example 13(a)**, (1.3 g, 5.0 mmol) provided the title product. MS (ESI, pos. ion) *m/z*: 223 (M+1).

(c). Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (1.3 g, 6.4 mmol, EMKA-Chemie) and ethyl 6-amino-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate, **Example 13(b)**, (1.4 g, 6.4 mmol) provided, after purification by silica gel chromatography (85:15 CH_2Cl_2:EtOAc), the title product as a pale yellow solid. MP 207–208 °C. MS (ESI, pos. ion) *m/z*: 409 (M+1).

Example 14

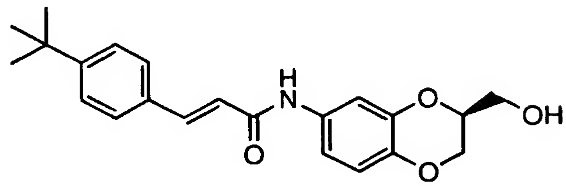


(2E)-3-[4-(tert-Butyl)phenyl]-N-[2-(hydroxymethyl)(2H,3H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl)]prop-2-enamide.

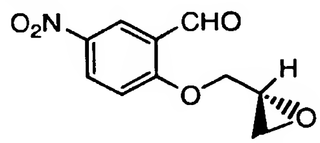
A solution of ethyl 6-{(2E)-3-[4-(*tert*-butyl)phenyl]prop-2-enoylamino}-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate, **Example 13,** (410 mg, 1.0 mmol) in THF (5 mL, Aldrich), magnetically stirred in a round-bottomed flask under N_2 at 0 °C, was treated with lithium borohydride (1.5 mL, 3.0 mmol, 2.0 M in THF, Aldrich). The reaction mixture was allowed to warm to 25 °C, and stirred at that temperature for 3 h. The reaction was quenched by the addition of satd NH_4Cl (5 mL), stirred for 30 min at 25 °C and extracted with EtOAc (2 x 15 mL). The combined organic extract was washed with satd NaCl, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (1:1

CH_2Cl_2:EtOAc) provided the title product as a pale yellow solid. MP 165–167 °C. MS (ESI, pos. ion) *m/z*: 367 (M+1).

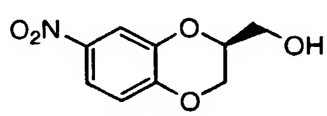
Example 15



(2E)-N-[(3S)-3-(Hydroxymethyl)(2H,3H-benzo[e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide.



(a) 2-[((2R)Oxiran-2-yl)methoxy]-5-nitrobenzaldehyde. A mixture of (*R*)-glycidyl tosylate (1.1 g, 5 mmol, Aldrich), 2-hydroxy-5-nitrobenzaldehyde (840 mg, 5.0 mmol, Aldrich) and solid K_2CO_3 (1.4 g, 10 mmol) in DMF (5 mL, Aldrich) was magnetically stirred in a round-bottomed flask at 100 °C under N_2 for 30 min. The reaction mixture was allowed to cool to 25 °C, water (20 mL) was added, and the mixture was extracted with EtOAc (3 x 30 mL). The combined extracts were washed with water (2 x 20 mL), satd NaCl (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (4:1 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 224 (M+1).

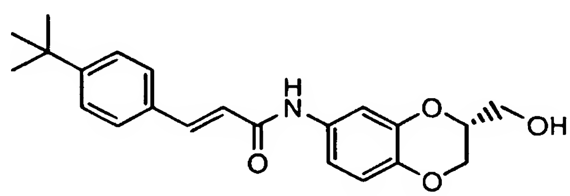


(b) ((2S)-7-Nitro-2H,3H-benzo[e]1,4-dioxan-2-yl)methan-1-ol. To a solution of 2-[((2R)oxiran-2-yl)methoxy]-5-nitrobenzaldehyde, **Example 15(a)**, (670 mg, 3.0 mmol) in CH_2Cl_2 (10 mL), magnetically stirred in a round-bottomed flask at 0 °C, was added 86% *m*-chloroperbenzoic acid (350 mg, 2.0 mmol, Aldrich). The reaction mixture was allowed to warm to 25 °C and stirred at that temperature for 18 h. The mixture was then diluted with CH_2Cl_2 (20 mL), washed with 10% $Na_2S_2O_3$ (3 mL), $NaHCO_3$ (3 x 5 mL), satd NaCl (3 mL), dried over Na_2SO_4,

filtered and concentrated in vacuo. The resulting residue was treated with MeOH (20 mL) and 1 N NaOH (6 mL) and stirred at 25 °C for 16 h. The reaction mixture was diluted with water (10 mL) and extracted with EtOAc (3 x 10 mL). The combined organic extracts were washed with satd NaCl, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (3:2 hexane:EtOAc) provided the product. MS (ESI, pos. ion) *m/z*: 212 (M+1).

(c) (2E)-N-[(3S)-3-(Hydroxymethyl)(2H,3H-benzo[e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide. A mixture of ((2S)-7-nitro-2H,3H-benzo[e]1,4-dioxan-2-yl)methan-1-ol, **Example 15(b),** (110 mg, 0.5 mmol) and 10% Pd on carbon (20 mg, Aldrich) in MeOH (5 mL), in a round-bottomed flask, was magnetically stirred under 1 atm H_2 for 2 h. The mixture was purged with N_2, filtered through a pad of Celite and concentrated in vacuo to provide the crude aniline [MS (ESI, pos. ion) *m/z*: 182 (M+1)]. Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (102 mg, 0.5 mmol, EMKA Chemie) and the crude aniline, provided the title product as a white solid. MP 169–171 °C. MS (ESI, pos. ion) *m/z*: 368 (M+1).

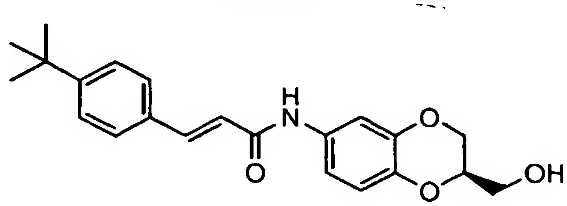
Example 16



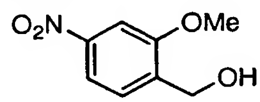
(2E)-N-[(3R)-3-(Hydroxymethyl)(2H,3H-benzo[e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide.

Analogous to the procedure described for **Example 15,** the title product was prepared starting from (*S*)-glycidyl tosylate (Aldrich), 2-hydroxy-5-nitrobenzaldehyde (Aldrich) and 4-*tert*-butyl-*trans*-cinnamic acid (EMKA Chemie). MP 170–171 °C. MS (ESI, pos. ion) *m/z*: 368 (M+1).

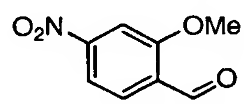
Example 17



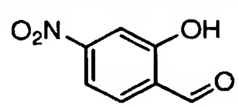
(2E)-N-[(2R)-2-(Hydroxymethyl)(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide.



(a) (2-Methoxy-4-nitrophenyl)methan-1-ol. To a solution of 2-methoxy-4-nitrobenzoic acid (2.0 g, 10 mmol, Aldrich) in THF (30 mL), magnetically stirred at 0 °C under N_2 in a round-bottomed flask equipped with a reflux condenser, was added borane-THF complex (30 mL, 30 mmol, 1.0 M in THF, Aldrich). The reaction mixture was stirred at reflux overnight. The reaction was quenched by the careful addition of MeOH (5 mL), followed by 1 N NaOH (30 mL). The mixture was extracted with EtOAc (2 x 50 mL), the combined organic extracts were washed with satd NaCl, dried over Na_2SO_4, filtered and concentrated in vacuo to give the product. MS (ESI, neg. ion) *m/z*: 182 (M−1).



(b) 2-Methoxy-4-nitrobenzaldehyde. A mixture of (2-methoxy-4-nitrophenyl)methan-1-ol, **Example 17(a),** (1.6 g, 8.9 mmol) and MnO_2 (15 g, 180 mmol, Aldrich) in 1:1 hexane: CH_2Cl_2 (60 mL) was magnetically stirred at 40 °C for 3 h. The solid was removed by filtration and washed with CH_2Cl_2. The filtrate was concentrated in vacuo and the residue was recrystallized from EtOAc and hexane to give the title product. MS (ESI, neg. ion) *m/z*: 180 (M−1).

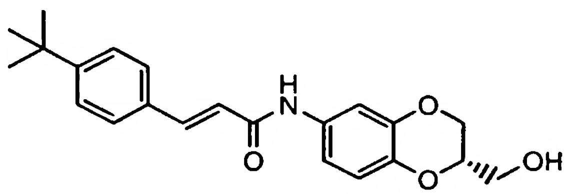


(c) 2-Hydroxy-4-nitrobenzaldehyde. To a solution of 2-methoxy-4-nitrobenzaldehyde, **Example 17(b),** (190 mg, 1.0 mmol) in CH_2Cl_2 (5 mL), magnetically stirred at –78 °C in a round-bottomed flask, was added BBr_3 (0.19 mL, 2.0 mmol, Aldrich). The reaction mixture was allowed to warm to 25 °C and stirred at that temperature for 2 h. The reaction mixture was then cooled to –78 °C, and treated with MeOH (5 mL). The mixture was allowed to warm to 25 °C, stirred at that temperature for 30 min, then concentrated in vacuo. Purification

by silica gel chromatography (3:2 hexane:EtOAc) provided 2-hydroxy-4-nitrobenzaldehyde. MS (ESI, neg. ion) *m/z*: 166 (M−1).

(d) (2E)-N-[(2R)-2-(Hydroxymethyl)(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure described for **Example 15**, the title product was obtained as a white solid from 2-hydroxy-4-nitrobenzaldehyde, **Example 17(c)**, (*S*)-glycidyl tosylate (Aldrich) and 4-*tert*-butyl-*trans*-cinnamic acid (EMKA-Chemie). MP 159–160 °C. MS (ESI, pos. ion) *m/z*: 368 (M+1).

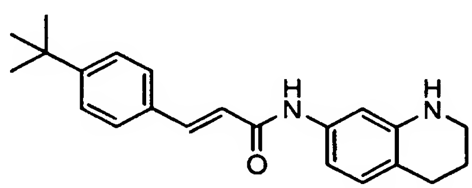
Example 18



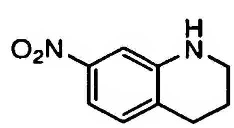
(2E)-N-[(2S)-2-(Hydroxymethyl)(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide.

Analogous to the procedure described for **Example 15,** the title product was prepared starting from 2-hydroxy-4-nitrobenzaldehyde, **Example 17(c)**, (*R*)-glycidyl tosylate (Aldrich) and 4-*tert*-butyl-*trans*-cinnamic acid (EMKA Chemie). MP 169–170 °C. MS (ESI, pos. ion) *m/z*: 368 (M+1).

Example 19

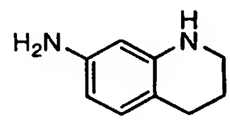


(2E)-3-[4-(tert-Butyl)phenyl]-N-(7-1,2,3,4-tetrahydroquinolyl)prop-2-enamide.



(a) 7-Nitro-1,2,3,4-tetrahydroquinoline. To a round-bottomed flask equipped with magnetic stirring was added 1,2,3,4-tetrahydroquinoline (6.3 mL, 50 mmol,

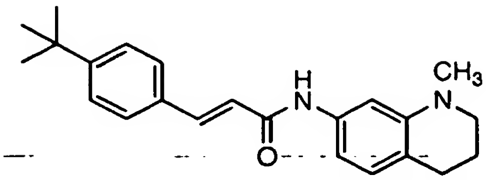
Aldrich) and 96% H_2SO_4 (42 mL). The mixture was stirred until all of the amine had dissolved, then cooled to 0 °C and treated with KNO_3 (5.9 g, 59 mmol) in portions. The reaction mixture was allowed to warm to 25 °C and stirred overnight at that temperature. The mixture was then cooled to 0 °C and neutralized with solid NaOH followed by 5 N NaOH until pH 11 was reached. The mixture was extracted with CH_2Cl_2 and the extract was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (8:1 hexane:EtOAc) provided 7-nitro-1,2,3,4-tetrahydroquinoline as an orange solid. MS (ESI, pos. ion) *m/z* 179 (M+1).



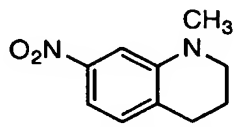
(b) 7-1,2,3,4-Tetrahydroquinolylamine. Analogous to the procedure used to prepare **Example 3(a)**, 7-nitro-1,2,3,4-tetrahydroquinoline, **Example 19(a)**, (0.35 g, 2.0 mmol) provided the aniline as a pale gray oil. MS (ESI, pos. ion) *m/z*: 149 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(7-1,2,3,4-tetrahydroquinolyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 7-1,2,3,4-tetrahydroquinolylamine, **Example 19(b)**, (280 mg, 1.9 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (0.33 g, 1.6 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (3:1 hexane:EtOAc) then recrystallization from EtOAc and hexane, the title product as a yellow solid. MP 225-227 °C. MS (ESI, pos. ion) *m/z*: 335 (M+1).

Example 20



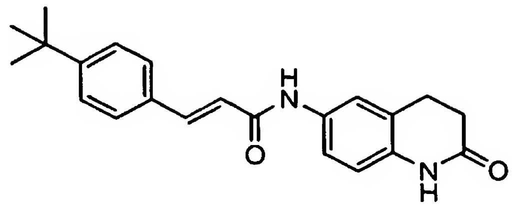
(2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methyl(7-1,2,3,4-tetrahydroquinolyl))-prop-2-enamide.



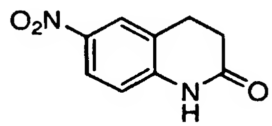
(a) 1-methyl-7-nitro-1,2,3,4-tetrahydroquinoline. To a solution of 7-nitro-1,2,3,4-tetrahydro-quinoline, **Example 19(a)**, (0.36 g, 2 mmol) in DMF (10 mL), magnetically stirred under N_2 at 0 °C in a 15 mL round-bottomed flask, was added sodium hydride (0.12 g, 3 mmol, 60% dispersion in mineral oil, Aldrich). After stirring for 10 min, the reaction mixture was treated with iodomethane (0.24 mL, 4 mmol, Aldrich) dropwise. The reaction mixture was stirred at 0 °C for 1 h, at 25 °C for an additional 1 h, then partitioned between EtOAc and satd NaCl. The aqueous layer was extracted with EtOAc (40 mL) and the combined organic extract was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (7:1 hexane:EtOAc) provided the product as an orange oil. MS (ESI, pos. ion) *m/z*: 193 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methyl(7-1,2,3,4-tetrahydroquinolyl))-prop-2-enamide. Analogous to the procedure described for **Example 19**, steps (b)-(c), 1-methyl-7-nitro-1,2,3,4-tetrahydroquinoline, **Example 20(a),** (240 mg, 1.3 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (0.23 g, 1.1 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (4:1 hexane:EtOAc) then recrystallization from EtOAc and hexane, the title product as a yellow solid. MP 200-202 °C. MS (ESI, pos. ion) *m/z*: 349 (M+1).

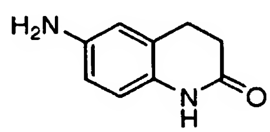
Example 21



(2E)-3-[4-(tert-Butyl)phenyl]-N-(2-oxo(6-1,3,4-trihydroquinolyl))prop-2-enamide.



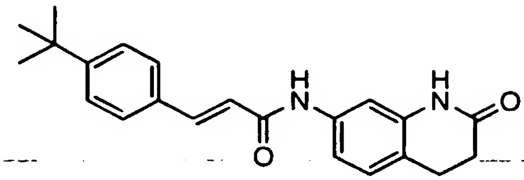
(a) 6-Nitro-1,3,4-trihydroquinolin-2-one. To a round-bottomed flask equipped with magnetic stirring was added 3,4-dihydro-2(1H)-quinolinone (1.47 g, 10 mmol, Aldrich) and 96% H_2SO_4 (8.3 mL). The mixture was stirred until all of the material was dissolved, then cooled to 0 °C and treated with KNO_3 (1.2 g, 11.7 mmol) in portions. The reaction mixture was allowed to warm to 25 °C and stirred at that temperature overnight. The mixture was basified to pH 9 with 35% NaOH, resulting in a precipitate. The solid was collected by filtration, washed with water and dried in vacuo at 50 °C to provide the title product as a yellow solid. MS (ESI, pos. ion) *m/z*: 193 (M+1).



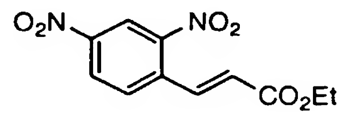
(b) 6-Amino-1,3,4-trihydroquinolin-2-one. Analogous to the procedure used to prepare **Example 3(a)**, 6-nitro-1,3,4-trihydroquinolin-2-one, **Example 21(a)**, (1.7 g, 8.9 mmol) was converted to the title product as a tan solid. MS (ESI, pos. ion) *m/z*: 163 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(2-oxo(6-1,3,4-trihydroquinolyl))prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 6-amino-1,3,4-trihydroquinolin-2-one, **Example 21(b)**, (0.68 g, 4.2 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (0.86 g, 4.2 mmol, EMKA-Chemie) provided, after recrystallization from MeOH, the title product as a pale yellow solid. MP 275-276 °C. MS (ESI, pos. ion) *m/z*: 349 (M+1).

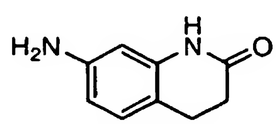
Example 22



(2E)-3-[4-(tert-Butyl)phenyl]-N-(2-oxo(7-1,3,4-trihydroquinolyl))prop-2-enamide.



(a) Ethyl 3-(2,4-dinitrophenyl)prop-2-enoate. A suspension of sodium hydride (2.0 g, 50 mmol, 60% dispersion in mineral oil, Aldrich) in anhydrous THF (100 mL) was magnetically stirred under N_2 at 25 °C and treated dropwise with triethyl phosphonoacetate (10 mL, 11 g, 51 mmol, Aldrich). The reaction mixture was stirred for 1 h at 25 °C then treated with 2,4-dinitrobenzaldehyde (9.0 g, 46 mmol, Aldrich) in portions. After stirring overnight at 25 °C, the reaction was quenched by the addition of water (50 mL) and concentrated in vacuo to remove the THF. The remaining aqueous mixture was extracted with EtOAc (2 x 150 mL). The combined organic extract was washed with water (4 x 100 mL), satd NaCl (75 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (1:4 hexane:EtOAc) provided the title product as a dark oil.

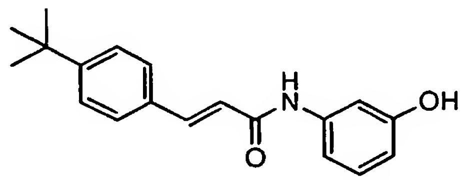


(b) 7-Amino-1,3,4-trihydroquinolin-2-one. Ethyl 3-(2,4-dinitrophenyl)prop-2-enoate, **Example 22(a)**, (3.0 g, 11 mmol) was dissolved in glacial acetic acid (240 mL), treated with 10% Pd on carbon (2.4 g, Aldrich) and hydrogenated on a Parr shaker apparatus at 65 °C, under 60 psi H_2, for 3 h. The reaction mixture was allowed to cool to 25 °C, purged with N_2, filtered through Celite and the filtercake washed with acetic acid (200 mL) and EtOH (200 mL). The combined filtrate was concentrated in vacuo, then treated with 1 N NaOH (150 mL) and extracted with EtOAc (3 x 100 mL). The combined organic extract was washed with satd

NaCl (50 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (EtOAc) provided the title product as a pale yellow solid. MS (ESI, pos. ion) *m/z*: 163 (M+1).

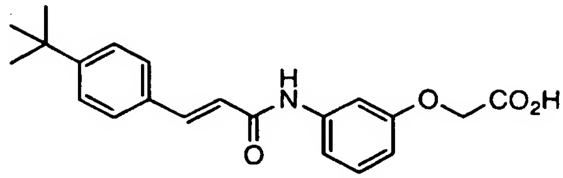
(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(2-oxo(7-1,3,4-trihydroquinolyl))prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 7-amino-1,3,4-trihydroquinolin-2-one, **Example 22(b)**, (300 mg, 1.8 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (370 mg, 1.8 mmol, EMKA-Chemie) provided the title product as white crystals. MP 288-290 °C. MS (ESI, pos. ion) *m/z*: 349 (M+1).

Example 23



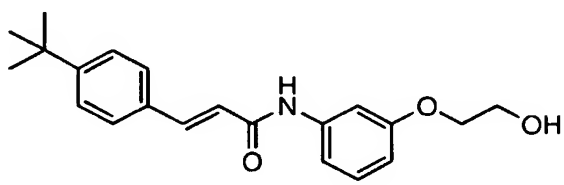
(2E)-3-[4-(tert-Butyl)phenyl]-N-(3-hydroxyphenyl)prop-2-enamide. To a round-bottomed flask equipped with magnetic stirring was added 4-*tert*-butyl-*trans*-cinnamic acid (530 mg, 2.43 mmol, EMKA-Chemie), CH_2Cl_2 (10 mL), and DMF (10 uL, Aldrich) under N_2. The solution was treated dropwise with oxalyl chloride (3.0 mL, 6.0 mmol, 2.0 M in CH_2Cl_2, Aldrich) then stirred at 25 °C for 1 h. The reaction mixture was concentrated in vacuo and treated with 3-aminophenol (265 mg, 2.43 mmol, Aldrich), THF (20 mL) and satd K_2CO_3 (15 mL). The reaction mixture was stirred at 25 °C overnight, then acidified to pH~4.5 with 1 N HCl. The mixture was extracted with EtOAc (2 × 30 mL), the combined organic extract was dried and concentrated in vacuo. Purification by silica gel chromatography (2:1 hexane:EtOAc) provided the title product as an oil. MS (ESI, pos. ion) m/z: 296 (M+1).

Example 24



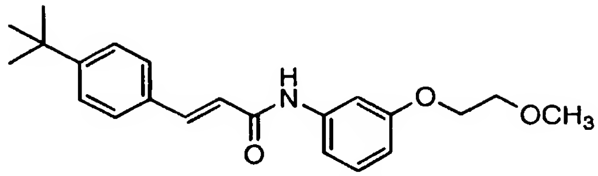
2-(3-{(2E)-3-[4-(tert-Butyl)phenyl]prop-2-enoylamino}phenoxy)acetic acid. To a round-bottomed flask equipped with magnetic stirring was added (2E)-3-[4-(*tert*-butyl)phenyl]-N-(3-hydroxyphenyl)prop-2-enamide, **Example 23**, (120 mg, 0.407 mmol), THF (10 mL), *tert*-butyl bromoacetate (60 uL, 0.407 mmol, Aldrich) and 5 N NaOH (10 mL). The reaction mixture was stirred at 25 °C overnight. The mixture was extracted with EtOAc (20 mL), the organic extract washed with water (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The resulting residue was treated with trifluoroacetic acid (10 mL), stirred at 25 °C for 2 h, then concentrated in vacuo. Purification by silica gel chromatography (1:2 hexane:EtOAc) provided the title product as an off-white solid. MP 166-172 °C. MS (ESI, pos. ion) m/z: 354 (M+1).

Example 25

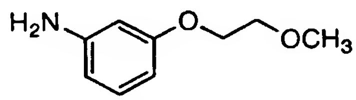


(2E)-3-[4-(tert-Butyl)phenyl]-N-[3-(2-hydroxyethoxy)phenyl]prop-2-enamide. To a round-bottomed flask, equipped with magnetic stirring and reflux condenser, was added (2E)-3-[4-(*tert*-butyl)phenyl]-N-(3-hydroxyphenyl)prop-2-enamide, **Example 23**, (200 mg, 0.68 mmol), THF (10 mL), 2-bromoethanol (200 uL, 2.80 mmol, Aldrich) and 5 N NaOH (10 mL). The reaction mixture was stirred at reflux for 5 h. After allowing to cool to 25 °C, the mixture was extracted with EtOAc (20 mL). The organic extract was washed with water (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (2:1 hexane:EtOAc) provided the title product as a colorless oil. MS (ESI, pos. ion) m/z: 340 (M+1).

Example 26



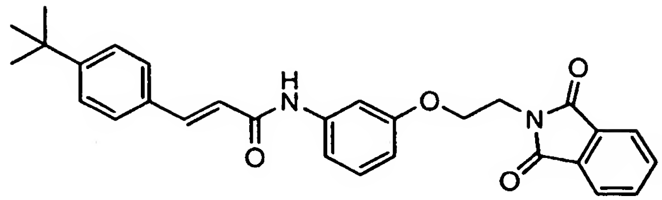
(2E)-3-[4-(tert-Butyl)phenyl]-N-[3-(2-methoxyethoxy)phenyl]prop-2-enamide.



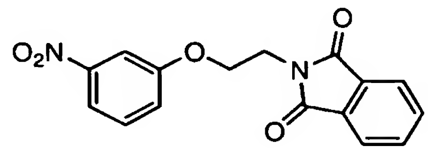
(a) 3-(2-Methoxyethoxy)phenylamine. To a round-bottomed flask equipped with magnetic stirring was added 3-aminophenol (1.2 g, 11 mmol, Aldrich), THF (15 mL) and sodium hydride (440 mg, 11 mmol, 60% in mineral oil, Aldrich) at 0 °C. The reaction mixture was allowed to stir at 0 °C for 30 min, then 2-bromoethyl methyl ether (1.0 mL, 11 mmol, Aldrich) was added dropwise. The reaction mixture was stirred at 25 °C overnight, then cooled to 0 °C and quenched with satd NaCl (10 mL). The mixture was extracted with EtOAc (20 mL) and the organic phase was washed with water (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide the title product. MS (ESI, pos. ion) m/z: 168 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-[3-(2-methoxyethoxy)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 2**, 3-(2-methoxyethoxy)phenylamine, **Example 26(a)**, (350 mg, 2.45 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (500 mg, 2.45 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (5:1 hexane:EtOAc), the title product as a colorless oil. MS (ESI, pos. ion) m/z: 354 (M+1).

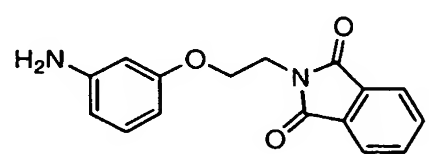
Example 27



(2E)-3-[4-(tert-Butyl)phenyl]-N-{3-[2-(1,3-dioxobenzo[c]azolin-2-yl)ethoxy]phenyl}prop-2-enamide.



(a) 2-[2-(3-Nitrophenoxy)ethyl]benzo[c]azoline-1,3-dione. To a round-bottomed flask, equipped with magnetic stirring, an addition funnel and a reflux condenser, was added 3-nitrophenol (2.0 g, 14 mmol, Fluka), triphenylphosphine (4.9 g, 19 mmol, Aldrich) and DMF (20 mL). A solution of N-[2-hydroxyethyl] phthalimide (2.7 mg, 14 mmol, Aldrich) and diethyl azodicarboxylate (3.3 g, 19 mmol, Aldrich) in DMF (20 mL) was added dropwise through the addition funnel at 25 °C. The reaction mixture was stirred at 60 °C for 12 h. The reaction mixture was concentrated in vacuo, dissolved in EtOAc (55 mL), and washed with satd NaCl (20 mL) and water (20 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (2:1 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) m/z: 313 (M+1).

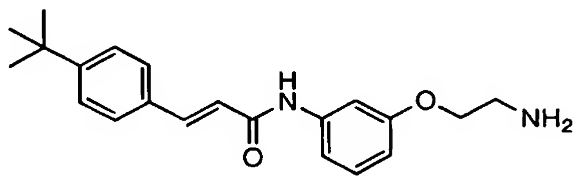


(b) 2-[2-(3-Aminophenoxy)ethyl]benzo[c]azoline-1,3-dione. In a round-bottomed flask, equipped with magnetic stirring, a solution of 2-[2-(3-nitrophenoxy)ethyl]benzo[c]azoline-1,3-dione, **Example 27(a)**, (1.9 g, 6.1 mmol) in 0.5% acetic acid in EtOAc (10 mL), under N_2, was treated with 10% Pd on carbon (500 mg, Aldrich). The suspension was purged with H_2 and stirred under 1 atm H_2 at 25 °C overnight. The suspension was purged with N_2 and filtered

through a pad of Celite. The solvent was removed in vacuo to provide the title product.

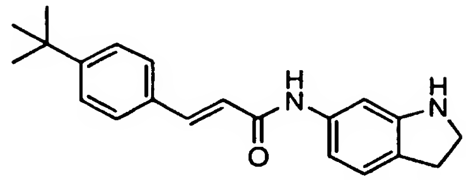
(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-{3-[2-(1,3-dioxobenzo[c]azolin-2-yl)ethoxy]phenyl}prop-2-enamide. Analogous to the procedure used to prepare **Example 2**, 2-[2-(3-aminophenoxy)ethyl]benzo[c]azoline-1,3-dione, **Example 27(b)**, (1.7 g, 6.1 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (1.2 g, 6.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (3:1 hexane:EtOAc), the title product as an off-white film. MS (ESI, pos. ion) m/z: 469 (M+1).

Example 28

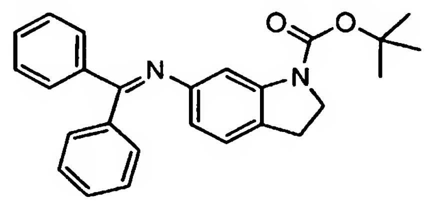


(2E)-N-[3-(2-Aminoethoxy)phenyl]-3-[4-(tert-butyl)phenyl]prop-2-enamide. To a round-bottomed flask equipped with magnetic stirring was added **Example 27,** (2E)-3-[4-(*tert*-butyl)phenyl]-N-{3-[2-(1,3-dioxobenzo[c]azolin-2-yl)ethoxy]phenyl}prop-2-enamide, (856 mg, 1.83 mmol), EtOH (15 mL) and hydrazine (574 uL, 18.3 mmol, Aldrich). The reaction mixture was stirred at 25 °C for 2 h. The mixture was concentrated in vacuo, the residue dissolved in EtOAc (40 mL), washed with 10% K_2CO_3 (15 mL), water (15 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (step gradient, EtOAc followed by 1:1 EtOAc:EtOH) provided the title product as an oil. MS (ESI, pos. ion) m/z: 339 (M+1).

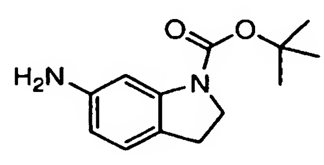
Example 29



(2E)-3-[4-(tert-Butyl)phenyl]-N-indolin-6-ylprop-2-enamide.



(a) tert-Butyl 6-(1-aza-2,2-diphenylvinyl)indolinecarboxylate. To a solution of benzophenone imine (0.91 g, 5.0 mmol, Aldrich) in CH_2Cl_2 (35 mL), magnetically stirred at 25 °C in a round-bottomed flask, was added a solution of 6-aminoindoline dihydrochloride (1.04 g, 5.0 mmol, Biosynth AG) in CH_2Cl_2 (40 mL). The reaction mixture was stirred at 25 °C for 12 h, then diluted with CH_2Cl_2 (30 mL), washed with water (30 mL), satd NaCl (30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. The crude product [MS (ESI, pos. ion) *m/z*: 299 (M+1)] was dissolved in 1,4-dioxane and treated with di-*tert*-butyl dicarbonate (8.0 mL, 8.0 mmol, 1.0 M in THF, Aldrich) and 5 N aq. Na_2CO_3 (5 mL). The reaction mixture was magnetically stirred at 25 °C until complete, then diluted with water (30 mL), and extracted with EtOAc (3 x 30 mL). The combined organic extract was washed with satd NaCl (30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (4:1 hexane EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 399 (M+1).

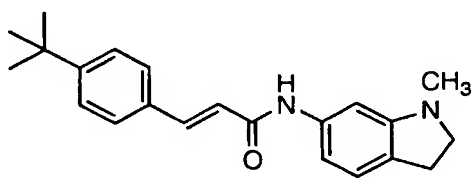


(b) tert-Butyl 6-aminoindolinecarboxylate. In a round-bottomed flask, a solution of *tert*-butyl 6-(1-aza-2,2-diphenylvinyl)indolinecarboxylate, **Example 29(a),** (0.80 g, 2.0 mmol) in 1,4-dioxane (10 mL) was treated with 1 N aq. HCl (10 mL). The reaction mixture was magnetically stirred overnight at 25 °C, then

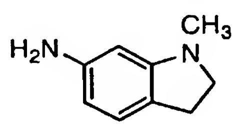
diluted with water (20 mL) and extracted with ethyl ether (30 mL). The aqueous phase was treated with 5 N NaOH (10 mL) and extracted with ethyl ether (3 x 30 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (3:2 hexane EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 235 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-indolin-6-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 1**, *tert*-butyl 6-aminoindoline-carboxylate, **Example 29(b),** (230 mg, 1.0 mmol) and 4-*tert*-butyl cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (7:3 hexane EtOAc), a crude product which was dissolved in CH_2Cl_2 (5 mL) and treated with 4 N HCl in dioxane (5 mL, Aldrich). The reaction mixture was magnetically stirred at 25 °C for 1 h, then washed with 5 N NaOH (15 mL), satd NaCl (15 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (55:45 hexane EtOAc) provided the title product. MP 153-167 °C. MS (ESI, pos. ion) *m/z*: 321 (M+1).

Example 30



(2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindolin-6-yl)prop-2-enamide.

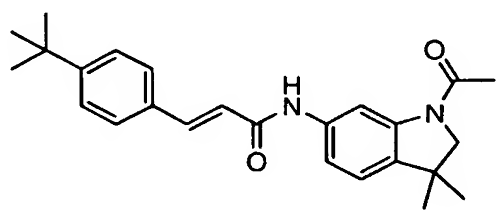


(a) 1-Methylindoline-6-ylamine. To a round-bottomed flask was added 6-nitroindoline (1.64 g, 10.0 mmol, Aldrich), 37% aq. formaldehyde (2.35 g, 30.0 mmol, Aldrich) and THF (40 mL). The reaction mixture was magnetically stirred at 25 °C and treated with sodium cyanoborohydride (1.89 g, 30.0 mmol, Aldrich). The reaction mixture was allowed to stir at 25 °C for 30 min, then washed with satd Na_2CO_3. The aqueous phase was extracted with ethyl ether, the organic phases combined and concentrated in vacuo to a residue. Analogous to the procedure of Goswami, P.; Chowdhury, P.; Indian J Chem, Sect B, **1997,** *36*

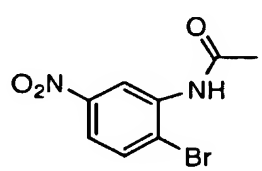
(2), 185-186, the crude residue was dissolved in tetrahydrofuran (60 mL) and added to Zn dust (0.43 g, 6.6 mmol, Aldrich) and $AlCl_3.6H_2O$ (9.6 g, 40 mmol, Aldrich) in water (2 mL), magnetically stirred at 25 °C. The reaction mixture was stirred at 25 °C for 16 h, then filtered. The filtrate was added to cold water (300 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extract was concentrated in vacuo to provide the title product as a brown solid. MS (ESI, pos. ion) *m/z*: 149 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindolin-6-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 1-methylindoline-6-ylamine, **Example 30(a)**, (150 mg, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) provided the title product as an amorphous yellow solid. MS (ESI, pos. ion) m/z: 335 (M+1).

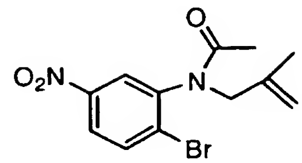
Example 31



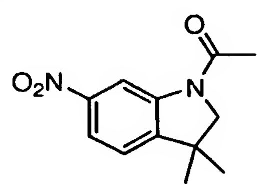
(2E)-N-(1-Acetyl-3,3-dimethylindolin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide.



(a) N-(2-Bromo-5-nitrophenyl)acetamide. A solution of 2-bromo-5-nitroaniline (43 g, 0.20 mol, Aldrich) in glacial acetic acid (1.3 L), magnetically stirred at 25 °C, was treated with acetic anhydride (20 mL, 0.21 mol). The reaction mixture was allowed to stir at 25 °C overnight, then quenched by pouring into water (6 L). The precipitate was collected by filtration, washed with water, and dried in vacuo to provide the title product as an off white solid. MS (ESI, pos. ion) *m/z*: 259, 262 (M+1, M+3).



(b) N-(2-Bromo-5-nitrophenyl)-N-(2-methylprop-2-enyl)acetamide. To a flame-dried round-bottomed flask, equipped with magnetic stirring and an addition funnel, was added N-(2-bromo-5-nitrophenyl)acetamide, **Example 31(a)**, (48 g, 0.19 mol), solid potassium carbonate (103 g, 744 mmol) and anhydrous DMF (830 mL). The resulting solution was stirred at 25 °C and treated dropwise, through the addition funnel, with a solution of 3-bromo-2-methylpropene (38 mL, 380 mmol, Aldrich) in anhydrous DMF (100 mL) over 45 min. The reaction mixture was stirred at 25 °C overnight, then filtered and treated with satd $NaHCO_3$. The organic layer was removed and the aqueous layer was extracted with EtOAc (3 x 150 mL). The combined organic extracts were washed with water (4 x 70 mL), satd NaCl (70 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to provide the title product as a golden solid. MS (ESI, pos. ion) *m/z*: 313, 315 (M+1, M+3).

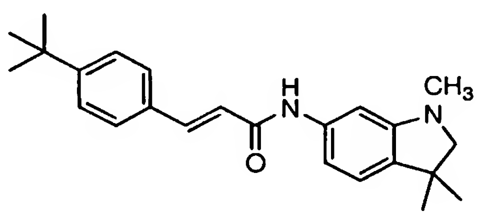


(c). 1-Acetyl-3,3-dimethyl-6-nitroindoline. To a flame-dried round-bottomed flask, equipped with magnetic stirring, was added N-(2-bromo-5-nitrophenyl)-N-(2-methylprop-2-enyl)acetamide, **Example 31(b)**, (55 g, 0.18 mol), tetraethylammonium chloride hydrate (30.8 g, 186 mmol, Aldrich), sodium formate (14.4 g, 212 mmol, Aldrich), sodium acetate (36.3 g, 443 mmol) and anhydrous DMF (443 mL). The resulting solution was purged with N_2 and treated with palladium (II) acetate (3.97 g, 17.7 mmol, Aldrich). The reaction mixture was stirred in an oil bath at 80 °C for 15 h, then allowed to cool to 25 °C and filtered through a pad of Celite. The Celite was washed with EtOAc and the combined filtrate was washed with satd $NaHCO_3$ (500 mL). The aqueous layer was extracted with EtOAc (3 x 100 mL) and the combined organic extract was washed with water (4 x 100 mL), satd NaCl (2 x 100 mL), dried over $MgSO_4$,

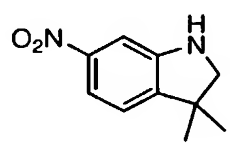
filtered and concentrated in vacuo to provide 1-acetyl-3,3-dimethyl-6-nitroindoline as a brown solid. MS (ESI, pos. ion) *m/z*: 235 (M+1).

(d) (2E)-N-(1-Acetyl-3,3-dimethylindolin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide. To a solution of 1-acetyl-3,3-dimethyl-6-nitroindoline, **Example 31(c)**, (110 mg, 0.47 mmol) in ethyl ether (3 mL), magnetically stirred in a round-bottomed flask at 0 °C, was added tin (II) chloride dihydrate (0.67 g, 2.96 mmol, Aldrich) and cond HCl (0.3 mL). The reaction mixture was stirred at 0 °C for 10 min, allowed to warm to 25 °C then stirred at that temperature overnight. The reaction mixture was washed with 10 N NaOH (10 mL), extracted with EtOAc and concentrated in vacuo. Analogous to the procedure used to prepare **Example 1**, the crude product and 4-*tert*-butyl-*trans*-cinnamic acid (92 mg, 0.45 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (2:3 hexane:EtOAc), the title product. MP 121 °C. MS (ESI, pos. ion) *m/z*: 391 (M+1).

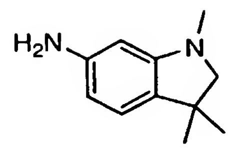
Example 32



(2E)-3-[4-(tert-Butyl)phenyl]-N-(1,3,3-trimethylindolin-6-yl)prop-2-enamide.



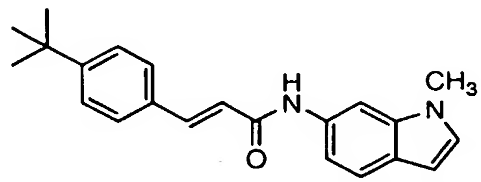
(a) 3,3-Dimethyl-6-nitroindoline. To a round-bottomed flask, equipped with magnetic stirring and a reflux condenser, was added 1-acetyl-3,3-dimethyl-6-nitroindoline, **Example 31(c)**, (1.73 g, 7.39 mmol) and EtOH (20 mL). The solution was treated with 12 N HCl (20 mL) then stirred and heated at reflux for 2 h. The reaction mixture was cooled to 0 °C, providing a precipitate which was collected by filtration and dried in vacuo to afford the title product as an off-white solid. MS (ESI, pos. ion) *m/z*: 193 (M+1).



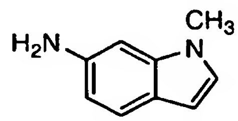
(b) 1,3,3-Trimethylindoline-6-ylamine. A solution of 3,3-dimethyl-6-nitroindoline, **Example 32(a)**, (0.23 g, 1.2 mmol) in anhydrous DMF (15 mL) was magnetically stirred at 25 °C and treated with sodium hydride (0.14 g, 3.6 mmol, 60% dispersion in mineral oil, Aldrich), followed by iodomethane (0.17, 1.3 mmol, Aldrich). The reaction mixture was stirred at 25 °C for 3 h, then quenched with water (40 mL) and extracted with EtOAc (3 x 30 mL). The combined extract was concentrated in vacuo to provide a residue [MS (ESI, pos. ion) *m/z*: 207 (M+1)] which was immediately dissolved in ethyl ether (5 mL), magnetically stirred at 0 °C, and treated with tin (II) chloride dihydrate (1.7 g, 7.5 mmol, Aldrich) and cond HCl (0.8 mL). The reaction mixture was stirred at 0 °C for 10 min, allowed to warm to 25 °C, then stirred at that temperature overnight. The reaction mixture was washed with 10 N NaOH (20 mL) and extracted with EtOAc (3 x 50 mL). The combined extracts were concentrated in vacuo and purified by silica gel chromatography to provide the title product. MS (ESI, pos. ion) *m/z*: 177 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1,3,3-trimethylindolin-6-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 1,3,3-trimethylindoline-6-ylamine, **Example 32(b)**, (176 mg, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (3:2 hexane:EtOAc), the title product. MP 90-101 °C. MS (ESI, pos. ion) *m/z*: 363 (M+1).

Example 33



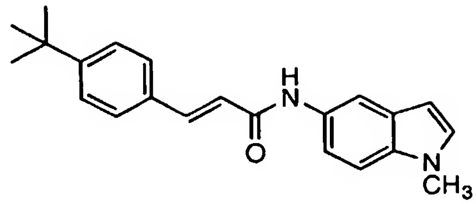
(2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindol-6-yl)prop-2-enamide.



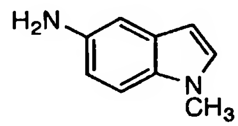
(a) 1-Methylindole-6-ylamine. To a round-bottomed flask was added 6-nitroindole (0.81 g, 5.0 mmol, Aldrich) and anhydrous DMF (40 mL). The solution was stirred magnetically and treated with sodium hydride (0.40 g, 10 mmol, 60% dispersion in mineral oil, Aldrich) followed by iodomethane (0.71 gm 10 mmol, Aldrich). Stirring was continued at 25 °C for 30 min, then the reaction mixture was quenched by the addition of water (75 mL) and extracted with EtOAc. The organic extract was concentrated in vacuo to provide a residue which was dissolved in EtOH (40 mL), treated with 10% Pd on carbon (400 mg, Aldrich), purged with H_2 and magnetically stirred under 1 atm H_2 for 4 h. The suspension was purged with N_2, filtered through a pad of Celite and concentrated in vacuo. Purification by silica gel chromatography (50:50 hexane:EtOAc) provided the aniline. MS (ESI, pos. ion) *m/z*: 147 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindol-6-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** 1-methylindole-6-ylamine, **Example 33(a),** (150 mg, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol), after purification by silica gel chromatography (65:35 hexane:EtOAc), provided the title product as a yellow solid. MP 95 °C. MS (ESI, pos. ion) *m/z*: 333 (M+1).

Example 34



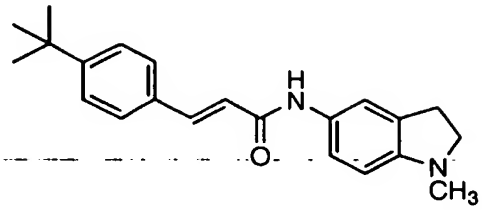
(2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindol-5-yl)prop-2-enamide.



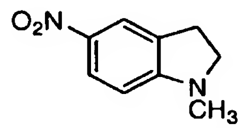
(a) 1-Methylindole-5-ylamine. To a round-bottomed flask was added 5-nitroindole (0.81 g, 5.0 mmol, Aldrich) and anhydrous DMF (40 mL). The solution was stirred magnetically and treated with sodium hydride (0.40 g, 10 mmol, 60% dispersion in mineral oil, Aldrich) followed by iodomethane (0.71 gm 10 mmol, Aldrich). Stirring was continued at 25 °C for 30 min, then the reaction mixture was quenched by the addition of water (75 mL) and extracted with EtOAc. The organic extract was concentrated in vacuo to provide a crude residue. Analogous to the procedure of Goswami, P.; Chowdhury, P.; *Indian J Chem, Sect B*, **1997**, *36* (2), 185-186, the crude residue was dissolved in THF (40 mL) and added to Zn dust (0.22 g, 3.3 mmol, Aldrich) and $AlCl_3 \cdot 6H_2O$ (4.78 g, 19.8 mmol, Aldrich) in water (1 mL), magnetically stirred at 25 °C. The reaction mixture was stirred at 25 °C for 16 h, then filtered. The filtrate was added to cold water (300 mL) and extracted with CH_2Cl_2 (3 x 100 mL). The combined organic extract was concentrated in vacuo to provide the title product. MS (ESI, pos. ion) *m/z*: 147 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindol-5-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 1-methylindole-5-ylamine, **Example 34(a)**, (150 mg, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (65:35 hexane:EtOAc), the title product as a crystalline yellow solid. MP 171 °C. MS (ESI, pos. ion) *m/z*: 333 (M+1).

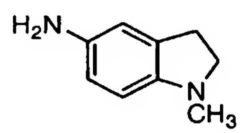
Example 35



(2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindolin-5-yl)prop-2-enamide.



(a) 1-Methyl-5-nitroindoline. To a round-bottomed flask equipped with magnetic stirring was added 5-nitroindoline (0.82, 5.0 mmol, Aldrich), iodomethane (0.71g, 5.0 mmol, Aldrich), sodium hydroxide (0.24, 6 mmol) and DMF (20 mL). The reaction mixture was stirred at 25 °C for 3 h, diluted with water (50 mL), extracted with EtOAc (3 x 40 mL) and the combined extracts were concentrated in vacuo. Purification by silica gel chromatography 97:3 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 179 (M+1).

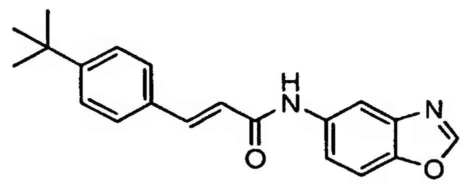


(b) 1-Methylindoline-5-ylamine. To a solution of 1-methyl-5-nitroindoline, **Example 35(a)**, (0.55 g, 3.1 mmol) in ethyl ether (20 mL), magnetically stirred in a round-bottomed flask at 0 °C, was added tin (II) chloride dihydrate (4.5 g, 20 mmol, Aldrich) and cond HCl (2.5 mL). The reaction mixture was stirred at 0 °C for 10 min, allowed to warm to 25 °C then stirred at that temperature overnight. The reaction mixture was washed with 10N NaOH (30 mL) and the aqueous phase extracted with EtOAc (3 x 20 mL). The combined organic extracts were concentrated in vacuo. Purification by silica gel chromatography (55:45 hexane:EtOAc) provided the aniline. MS (ESI, pos. ion) *m/z*: 149 (M+1).

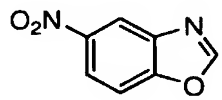
(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-(1-methylindolin-5-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 1-methylindoline-5-ylamine, **Example 35(b)**, (150, 1.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid

(200 mg, 1.0 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (60:40 hexane:EtOAc), the title product as a crystalline yellow solid. MP 194 °C. MS (ESI, pos. ion) *m/z*: 335 (M+1).

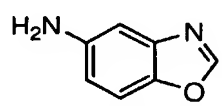
Example 36



(2E)-N-Benzoxazol-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide.



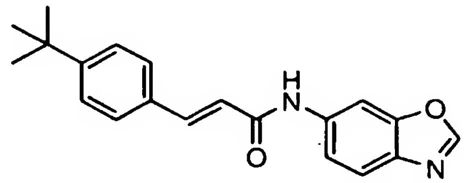
(a) 5-Nitrobenzoxazole. Following the procedure of A. R. Katritzky et al. *Heterocycles* **1995**, *41*, 345, to a round-bottomed flask was added 2-amino-4-nitrophenol (5.0 g, 32 mmol, Aldrich), trimethyl orthoformate (20 mL, 180 mmol, Aldrich) and *p*-toluenesulfonic acid monohydrate (300 mg, 1.6 mmol, Aldrich). The reaction mixture was magnetically stirred in a 95 °C oil bath for 1 h, and then allowed to cool to 25 °C. The mixture was cooled to 0 °C to provide a precipitate which was collected by filtration, washed with cold toluene, pentane, then dried in vacuo to afford the title product as a dark brown powder.



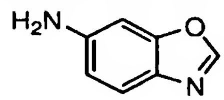
(b) Benzoxazole-5-ylamine. Analogous to the procedure used to prepare **Example 3(a),** 5-nitrobenzoxazole, **Example 36(a),** (2.4 g, 15 mmol) provided, after purification by silica gel chromatography (step gradient, 7:3 then 4.5:5.5 then 3:7 hexane:EtOAc), the title product. MS (ESI, pos. ion) *m/z*: 135 (M+1).

(c) (2E)-N-Benzoxazol-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, benzoxazole-5-ylamine, **Example 36(b)**, (530 mg, 4.0 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (820 mg, 4.0 mmol, EMKA-Chemie) provided, after twice being purified by silica gel chromatography (7:3 hexane:EtOAc then 1.25% MeOH in CH_2Cl_2), the title product as white crystals. MP 177 °C. MS (ESI, pos. ion) *m/z*: 321 (M+1).

Example 37



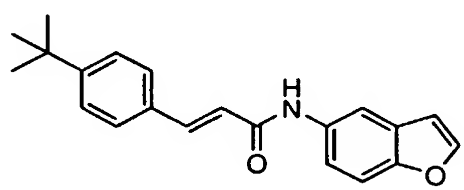
(2E)-N-Benzoxazol-6-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide.



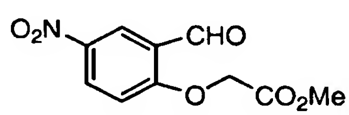
(a) Benzoxazole-6-ylamine. Analogous to the procedure described for the preparation of **Example 36,** steps (a)-(b), 2-amino-5-nitrophenol (5.0 g, 32 mmol, Aldrich) provided the title product as a pale tan solid. MS (ESI, pos. ion) *m/z*: 135 (M+1).

(b) (2E)-N-Benzoxazol-6-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** benzoxazole-6-ylamine, **Example 37(a),** (1.8 g, 13 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (2.7 g, 13 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (6:4:0.2 CH_2Cl_2:hexane:MeOH), the title product as a tan solid. MP 147-148 °C. MS (ESI, pos. ion) *m/z*: 321 (M+1).

Example 38

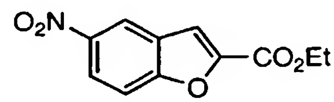


(2E)-N-Benzo[b]furan-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide.

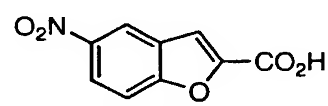


(a) Methyl 2-(2-formyl-4-nitrophenoxy)acetate. To a round-bottomed flask was added a suspension of 2-hydroxy-5-nitrobenzaldehyde (10 g, 60 mmol, Aldrich) in anhydrous EtOH (180 mL). The suspension was treated with KOH (4.4 g, 66 mmol) and heated under N_2 with magnetic stirring in a 65 °C oil bath for 45 min. The reaction mixture was allowed to cool to 25 °C and concentrated in vacuo. Anhydrous DMF (180 mL) was added, and the reaction flask was

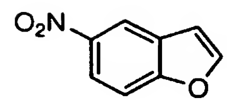
cooled in an ice bath and charged with methyl bromoacetate (10 mL, 110 mL, Aldrich). The reaction mixture was stirred for 3.5 h at 25 °C, then the solvent was removed in vacuo. Water (200 mL) was added, and the mixture was extracted with EtOAc (3 × 50 mL). The combined organic extract was washed with 1 M H_3PO_4, satd $NaHCO_3$, and satd NaCl. After drying over $MgSO_4$, the organic layer was filtered and concentrated in vacuo. The residue was recrystallized from CH_2Cl_2 and hexane to afford the title product as a pale yellow solid. MS (ESI, pos. ion) *m/z*: 240 (M+1).



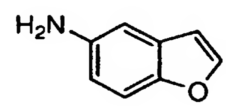
(b) Ethyl 5-nitrobenzo[d]furan-2-carboxylate. To a 250 mL round-bottomed flask was added methyl 2-(2-formyl-4-nitrophenoxy)acetate, **Example 38(a),** (5.3 g, 22 mmol), EtOH (110 mL) and 1,8-diazabicyclo[5.4.0]undec-7-ene (3.7 g, 24 mmol, Aldrich). The reaction mixture was magnetically stirred at 25 °C for 20 h, then concentrated to approximately half of its volume in vacuo. After cooling the mixture in an ice bath for 20 min, a precipitate formed which was collected by filtration and washed with ice cold EtOH. The resulting pale yellow solid was dried in vacuo to provide the title product. MS (ESI, pos. ion) *m/z*: 253 ($M+H_2O$).



(c) 5-Nitrobenzo[b]furan-2-carboxylic acid. To a 250 mL round-bottomed flask was added ethyl 5-nitrobenzo[d]furan-2-carboxylate, **Example 38(b),** (1.0 g, 4.3 mmol), EtOH (10 mL), and KOH (610 mg, 11 mmol) in 10 mL of H_2O. The reaction mixture was stirred at 25 °C for 24 h, then treated with 1 M H_3PO_4 (200 mL) and saturated with solid NaCl. The aqueous layer was extracted with EtOAc (3 × 70 mL), and the combined organic extracts were washed with satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo to provide the title product as a yellowish-white powder. MS (ESI, pos. ion) *m/z*: 225 ($M+H_2O$).



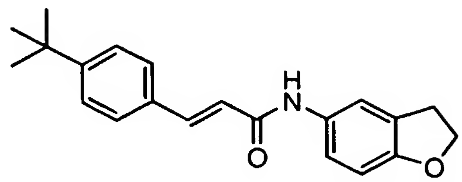
(d). 5-Nitrobenzofuran. To a 100 mL round-bottomed flask was added 5-nitrobenzo[b]furan-2-carboxylic acid, **Example 38(c),** (860 mg, 4.2 mmol), copper (830 mg, 13 mmol, Aldrich), and quinoline (38 mL, Aldrich). The reaction flask was placed in a 185 °C oil bath and magnetically stirred for 20 min under N_2. After allowing to cool to 25 °C, the mixture was filtered through a 1" pad of Celite. To the filtrate was added 10% aq. HCl (300 mL) and the aqueous layer was extracted with Et_2O (3 × 100 mL). The combined ethereal layers were washed with 10% HCl (4 × 200 mL, 1 × 100 mL), satd $NaHCO_3$ (200 mL), and satd NaCl (100 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (10:0.25 hexanes:EtOAc) provided 5-nitrobenzofuran as a white solid.



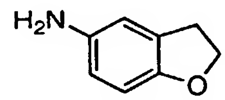
(e) Benzo[b]furan-5-ylamine. To a 150 mL round-bottomed flask was added 5-nitrobenzofuran, **Example 38(d)**, (270 mg, 1.7 mmol) and ethyl ether (16 mL). The mixture was magnetically stirred at 0 °C under N_2 and treated with a solution of tin (II) chloride dihydrate (3.4 g, 15 mmol, Aldrich) in 12 M aq. HCl (2 mL). The reaction mixture was stirred at 0 °C for 10 min, then allowed to warm to 25 °C and stirred at that temperature for 20 h. Water and 2 N NaOH (pH > 10) were added followed by Celite (10 g). The mixture was filtered through a pad of Celite and the filtrate extracted with EtOAc. The organic extract was washed with 2 N NaOH, satd NaCl, dried over K_2CO_3, filtered and concentrated in vacuo to provide the title product as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 134 (M+1).

(f) (2E)-N-Benzo[b]furan-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, benzo[b]furan-5-ylamine, **Example 38(e),** (230 mg, 1.7 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (350 mg, 1.7 mmol, EMKA-Chemie) provided, after purification by silica gel chromatography (9:1 hexane:EtOAc), the title product as white crystals. MP 149-150 °C. MS (ESI, pos. ion) *m/z*: 320 (M+1).

Example 39



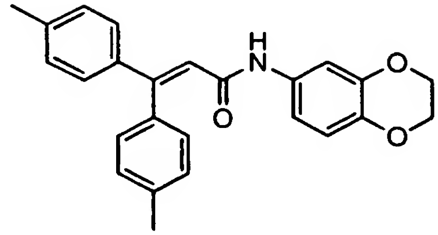
(2E)-3-[4-(tert-Butyl)phenyl]-N-(2,3-dihydrobenzo[b]furan-5-yl)prop-2-enamide.



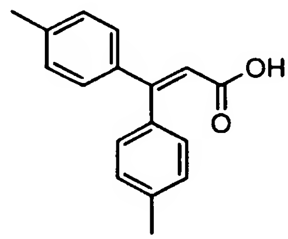
(a) 2,3-Dihydrobenzo[b]furan-5-ylamine. To a 150 mL round-bottomed flask was added 5-nitrobenzofuran, **Example 38(d)**, (250 mg, 1.5 mmol), EtOAc (16 mL) and 10% Pd on carbon (33 mg, Aldrich). The suspension was stirred at 25 °C under 1 atm H_2 for 24 h, then purged with N_2, filtered through Celite and concentrated in vacuo to provide the aniline as a red-brown solid. MS (ESI, pos. ion) *m/z*: 136 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-(2,3-dihydrobenzo[b]furan-5-yl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 2,3-dihydrobenzo[b]furan-5-ylamine, **Example 39(a),** (240 mg, 1.8 mmol) and 4-*tert*-butyl-*trans*-cinnamic acid (370 mg, 1.8 mmol, EMKA-Chemie) provided the crude title product. The product was purified by silica gel chromatography (9:1:0.25 hexane:EtOAc:MeOH) to provide 45 mg of the title product and additional impure fractions. The impure fractions were combined and concentrated in vacuo. The residue was dissolved in MeOH (25 mL), treated with 5 N NaOH (10 mL) and stirred for 1 h. The mixture was diluted with 5 N NaOH (100 mL) and extracted with EtOAc. The organic phase was washed with 5 N NaOH (2 x), 5% citric acid, satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (8:1:0.5 hexane:EtOAc: 2 M NH_3 in MeOH) provided an additional the title product as a white solid. MP 175-176 °C. MS (ESI, pos. ion) *m/z*: 322 (M+1).

Example 40



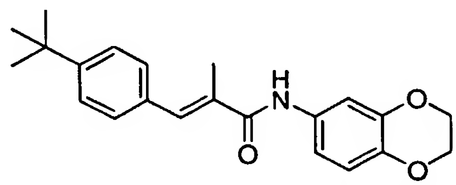
N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3,3-bis(4-methylphenyl)prop-2-enamide.



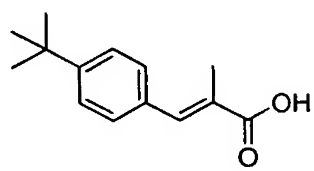
(a) 3,3-Bis(4-methylphenyl)prop-2-enoic acid. Triethyl phosphonoacetate (2.0 mL, 10 mmol, Aldrich) was added dropwise to a suspension of NaH (0.44 g, 11 mmol, 60% dispersion in mineral oil, Aldrich) in anhydrous THF (16 mL), magnetically stirred at 0 °C under Ar, in a round-bottomed flask equipped with a reflux condenser. The reaction mixture was allowed to warm to 25 °C then stirred at that temperature for 0.5 h. 4,4'-Dimethylbenzophenone (2.1 g, 10 mmol, Aldrich) was added in one portion and the reaction mixture stirred and heated at reflux for 48 h. After allowing to cool to 25 °C, the reaction mixture was quenched with H_2O (30 mL) and extracted with Et_2O (4 x 10 mL). The combined organic extract was washed with H_2O (5 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to an oily residue. The residue was dissolved in 1,4-dioxane (2.5 mL), treated with H_2O (7 mL) and KOH (1.1 g, 20 mmol), then stirred and heated at reflux under Ar for 18 h. The reaction mixture was allowed to cool to 25 °C, diluted with H_2O (50 mL) and washed with Et_2O (10 mL). The aqueous phase was acidified with 1 N HCl and extracted with chloroform. The combined chloroform extracts were washed with satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo to provide the acid as a white solid. MS (ESI, pos. ion) *m/z*: 253 (M+1).

(b) N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3,3-bis(4-methylphenyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 3,3-bis(4-methylphenyl)prop-2-enoic acid, **Example 40(a)**, (0.50 g, 2.0 mmol) and 1,4-benzodioxan-6-amine (0.33 g, 2.2 mmol, Aldrich) provided, after purification by silica gel chromatography (chloroform), the title product as a yellow solid. MP 163–164 °C. MS (ESI, pos. ion) *m/z*: 386 (M+1).

Example 41



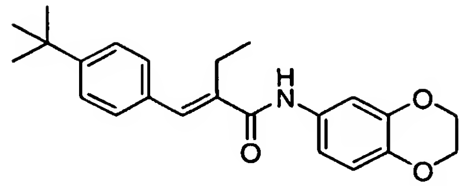
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-methylprop-2-enamide.



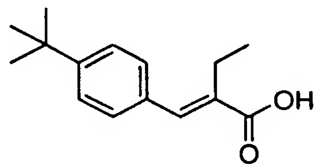
(a) (2E)-3-[4-(tert-Butyl)phenyl]-2-methylprop-2-enoic acid. Analogous to the procedure described for the preparation of **Example 40**, step (a), triethyl 2-phosphonopropionate (2.4 g, 10 mmol, Aldrich) and 4-*tert*-butylbenzaldehyde (1.6 g, 10 mmol, Aldrich) provided the title product as a yellow solid. MS (ESI, pos. ion) *m/z*: 219 (M+1).

(b) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-methylprop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[4-(*tert*-butyl)phenyl]-2-methylprop-2-enoic acid, **Example 41(a)**, (0.44 g, 2.0 mmol) and 1,4-benzodioxan-6-amine (0.33 g, 2.2 mmol, Aldrich) provided, after purification by silica gel chromatography (chloroform), the title product as an off-white solid. MP 157–158 °C. MS (ESI, pos. ion) *m/z*: 352 (M+1).

Example 42



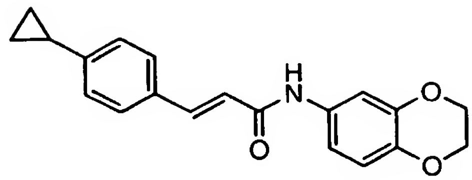
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-ethylprop-2-enamide.



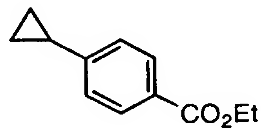
(a) (2E)-3-[4-(tert-Butyl)phenyl]-2-ethylprop-2-enoic acid. Analogous to the procedure described for the preparation of **Example 40**, step (a), triethyl 2-phosphonobutyrate (2.5 g, 10 mmol, Aldrich) and 4-*tert*-butylbenzaldehyde (1.6 g, 10 mmol, Aldrich) provided the title product as a white solid. MS (ESI, pos. ion) *m/z*: 233 (M+1).

(b) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-ethylprop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[4-(*tert*-butyl)phenyl]-2-ethylprop-2-enoic acid, **Example 42(a),** (0.46 g, 2.0 mmol) and 1,4-benzodioxan-6-amine (0.33 g, 2.2 mmol, Aldrich) provided, after purification by silica gel chromatography (chloroform), the title product as a white solid. MP 133–134 °C. MS (ESI, pos. ion) *m/z*: 366 (M+1).

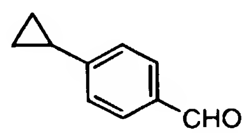
Example 43



(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-(4-cyclopropylphenyl)prop-2-enamide.

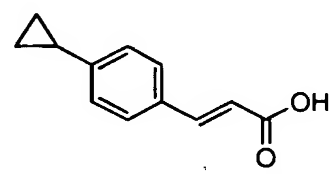


(a) Ethyl 4-cyclopropylbenzoate. To a round-bottomed flask under N_2 was added zinc dust (0.80 g, 12.5 mmol, Aldrich), cuprous chloride (1.23 g, 12.5 mmol, Aldrich) and Et_2O (2 mL). The mixture was magnetically stirred and heated at reflux for 30 min. The suspension was treated with ethyl 4-vinylbenzoate (0.85 g, 4.82 mmol, Apin) followed by methylene diiodide (1.68 g, 6.27 mmol, Aldrich) and reflux was continued for 24 h. The reaction mixture was allowed to cool to 25 °C, filtered, concentrated in vacuo and purified by silica gel chromatography (9:1 hexane:EtOAc) to provide the title product. MS (ESI, pos. ion) *m/z*: 191 (M+1).



(b) 4-Cyclopropylbenzaldehyde. Ethyl 4-cyclopropylbenzoate, **Example 43(a),** (316 mg, 1.66 mmol) was transferred to a round-bottomed flask and treated with lithium aluminum hydride (0.30 mL, 3.0 mmol, 1.0 M in THF, Aldrich) under N_2. The reaction mixture was magnetically stirred at 25 °C for 1 h, then quenched by the dropwise addition of H_2O (0.5 mL) followed by 20% aq. KOH (3 mL). The suspension was filtered and the aqueous phase extracted with EtOAc. The organic extract was concentrated in vacuo and the crude alcohol was redissolved in anhydrous CH_2Cl_2 (2 mL). In a separate round-bottomed flask, a solution of oxalyl chloride (2.0 mL, 4.0 mmol, 2.0 M in CH_2Cl_2, Aldrich) was magnetically stirred under N_2 at –78 °C and treated dropwise with a solution of anhydrous

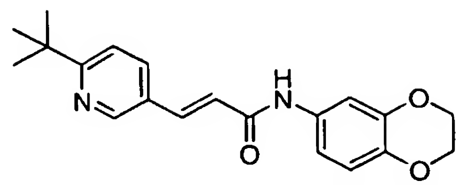
dimethyl sulfoxide (4.0 mL, 56 mmol, Aldrich) in anhydrous CH_2Cl_2 (2 mL). The reaction mixture was stirred at –78 °C for 5 min then treated dropwise with the solution of crude alcohol in CH_2Cl_2. The reaction mixture was stirred an additional 5 min at –78 °C, treated with triethylamine (2.0 mL, 14 mmol), allowed to warm to 25 °C and stirred at that temperature for 1 h. The reaction was quenched by the addition of H_2O and the mixture was extracted with Et_2O. The organic extract was concentrated in vacuo to provide 230 mg (95% over two steps) of the title product.



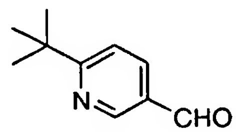
(c) (2E)-3-(4-Cyclopropylphenyl)prop-2-enoic acid. Analogous to the procedure described for **Example 40,** step (a), 4-cyclopropylbenzaldehyde, **Example 43(b),** (0.23 g, 1.6 mmol) and triethyl phosphonoacetate (0.35 g, 1.6 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 189 (M+1).

(d) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-(4-cyclopropylphenyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-(4-cyclopropylphenyl)prop-2-enoic acid, **Example 43(c),** (130 mg, 0.69 mmol) and 1,4-benzodioxan-6-amine (104 mg, 0.69 mmol, Aldrich) provided, after purification by silica gel chromatography (65:35 hexane:EtOAc), the title product as a clear glass. MS (ESI, pos. ion) *m/z*: 322 (M+1).

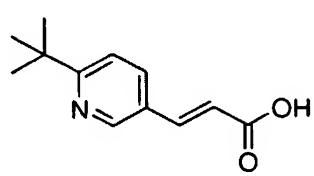
Example 44



(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)(3-pyridyl)]-prop-2-enamide.



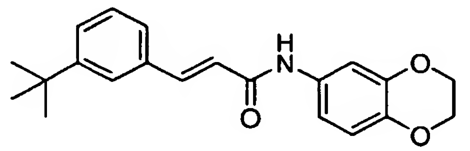
(a) 6-(tert-Butyl)pyridine-3-carbaldehyde. Analogous to the procedure of Rybakova, et al. *Zh. Org. Khim.* **1995**, *31*(5), 670-673, pyridine-3-methanol (2.18 g, 20.0 mmol, Aldrich), trimethylacetic acid (10.2 g, 100 mmol, Aldrich), silver nitrate (0.68 gm 4.0 mmol, Aldrich), and 10% aq. sulfuric acid (20 mL) were combined in a round-bottomed flask. The reaction mixture was magnetically stirred and treated with a solution of ammonium persulfate (9.1 g, 40 mmol, Aldrich) in H_2O (40 mL). Evolution of gas was observed and the reaction mixture was stirred at 25 °C for 2 h. The reaction mixture was basified to pH 9 by the addition of aq. ammonium hydroxide then extracted with EtOAc. The organic extract was washed with H_2O, dried over Na_2SO_4, filtered and concentrated in vacuo. Purification of the crude product by silica gel chromatography (70:30 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 164 (M+1).



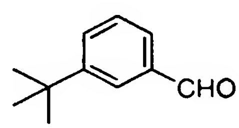
(b) (2E)-3-[6-(tert-Butyl)(3-pyridyl)]prop-2-enoic acid. Analogous to the procedure described for **Example 40,** step (a), 6-(*tert*-butyl)pyridine-3-carbaldehyde, **Example 44(a),** (0.55 g, 3.4 mmol) and triethyl phosphonoacetate (0.76 g, 3.4 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 206 (M+1).

(c) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)(3-pyridyl)]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)(3-pyridyl)]prop-2-enoic acid, **Example 44(b),** (200 mg, 1.0 mmol) and 1,4-benzodioxan-6-amine (150 mg, 1.0 mmol, Aldrich) provided, after purification by silica gel chromatography (60:40 hexane:EtOAc), the title product as a clear glass. MS (ESI, pos. ion) *m/z*: 339 (M+1).

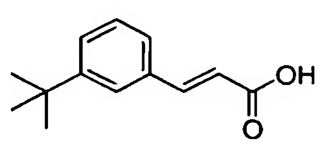
Example 45



(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[3-(tert-butyl)phenyl]prop-2-enamide.



(a) 3-(tert-Butyl)benzaldehyde. To a round-bottomed flask equipped with magnetic stirring was added 1-*tert*-butyl-3-methylbenzene (1 g, 6.8 mmol, Wiley), ammonium cerium (IV) nitrate (17.5 g, 29.7 mmol, Aldrich) and 50% aq. acetic acid (150 mL). The reaction mixture was stirred and heated at 90 °C for 1.5 h. The reaction mixture was allowed to cool to 25 °C and extracted with 10% EtOAc in hexane. The organic extract was concentrated in vacuo to provide the crude aldehyde.

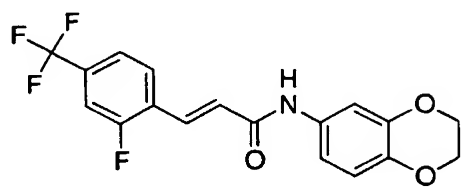


(b) (2E)-3-[3-(tert-Butyl)phenyl]prop-2-enoic acid. Analogous to the procedure described for **Example 40,** step (a), 3-(*tert*-butyl)benzaldehyde, **Example 45(a),** (320 mg, 2.0 mmol) and triethyl phosphonoacetate (250 mg, 2.0 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 205 (M+1).

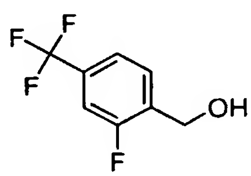
(c) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[3-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** (2E)-3-[3-

(*tert*-butyl)phenyl]prop-2-enoic acid, **Example 45(b),** (200 mg, 1.0 mmol) and 1,4-benzodioxan-6-amine (150 mg, 1.0 mmol, Aldrich) provided, after purification by silica gel chromatography (60:40 hexane:EtOAc), the title product. MP 168 °C. MS (ESI, pos. ion) *m/z*: 338 (M+1).

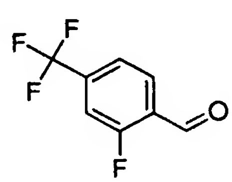
Example 46



(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[2-fluoro-4-(trifluoromethyl)-phenyl]prop-2-enamide.

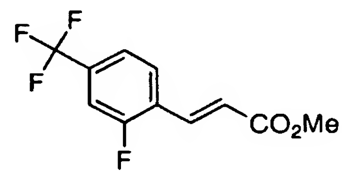


(a) [2-Fluoro-4-(trifluoromethyl)phenyl]methan-1-ol. To a round-bottomed flask, equipped with magnetic stirring and a reflux condenser, was added 2-fluoro-4-(trifluoromethyl)benzoic acid (5.0 g, 24 mmol, ABCR) and borane-THF complex (72 mL, 72 mmol, 1.0 M in THF, Aldrich) at 0 °C under N_2. The reaction mixture was warmed to 65 °C and stirred at that temperature for 2 h. The reaction mixture was allowed to cool to 25 °C and the solvent was removed in vacuo. The resulting residue was dissolved in CH_2Cl_2 (100 mL) and washed with satd Na_2CO_3 (100 mL). The aqueous phase was back-extracted with CH_2Cl_2 (4 x 80 mL). The combined organic extract was washed with satd NaCl (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (gradient: 0-10% EtOAc in hexane) provided the title product as a colorless oil.

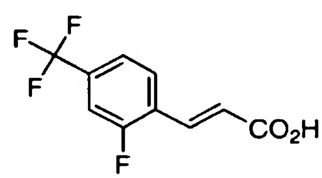


(b) 2-Fluoro-4-(trifluoromethyl)benzaldehyde. To a solution of [2-fluoro-4-(trifluoromethyl)phenyl]methan-1-ol, **Example 46(a),** (4.4 g, 23 mmol) in CH_2Cl_2

(100 mL) was added ground pyridinium dichromate (38.4 g, 102 mmol, Fluka). The reaction mixture was stirred at 25 °C overnight, then filtered through Celite. The Celite pad was washed with CH_2Cl_2 (2 x 50 mL) and the combined filtrate was concentrated in vacuo. Purification by silica gel chromatography (gradient: 0-5% EtOAc in hexane) provided the title product as a white slurry.



(c) Methyl (2E)-3-[2-fluoro-4-(trifluoromethyl)phenyl]prop-2-enoate. 2-Fluoro-4-(trifluoromethyl)benzaldehyde, **Example 46(b),** (900 mg, 4.7 mmol) in CH_2Cl_2 (5 mL) was added via cannula to a solution of carbomethoxymethylene triphenylphosphorane (2.0 g, 6.1 mmol, Aldrich) in CH_2Cl_2 (15 mL), magnetically stirred in a round-bottomed flask at 0 °C. The reaction mixture was allowed to warm to 25 °C and stirred at this temperature under N_2 overnight. The solvent was removed in vacuo and the crude material purified by silica gel chromatography (gradient: 0-5% EtOAc in hexane) to provide the title product as a white solid.

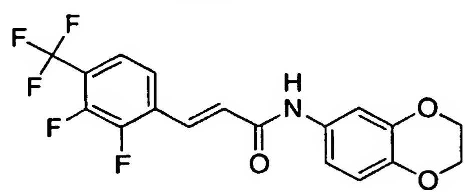


(d) (2E)-3-[2-Fluoro-4-(trifluoromethyl)phenyl]prop-2-enoic acid. Methyl (2E)-3-[2-fluoro-4-(trifluoromethyl)phenyl]prop-2-enoate, **Example 46(c),** (1.6 g, 6.3 mmol) was treated with lithium hydroxide monohydrate (530 mg, 12.6 mmol, Aldrich) in wet EtOH (15 mL) and magnetically stirred in a round-bottomed flask at 25 °C overnight. The reaction mixture was acidified to pH < 2 with 10% aq. HCl and extracted with EtOAc (3 x 50 mL). The combined extracts were washed with satd NaCl (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide the acid as a white solid.

(e) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[2-fluoro-4-(trifluoromethyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-fluoro-4-(trifluoromethyl)phenyl]prop-2-enoic

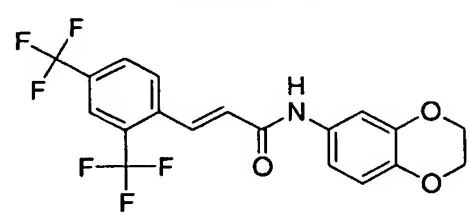
acid, **Example 46(d)**, (200 mg, 0.85 mmol) and 1,4-benzodioxan-6-amine (193 mg, 1.28 mmol, Aldrich) provided, after purification by silica gel chromatography (gradient: 0-20% EtOAc in hexane) and recrystallization from EtOAc and hexane, the title product as a yellow crystalline solid. MP 174-175 °C. MS (ESI, pos. ion) m/z: 368 (M+1).

Example 47



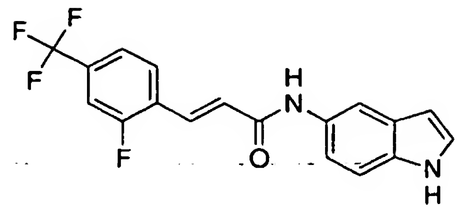
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[2,3-difluoro-4-(trifluoromethyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 46**, steps (b)-(e), the title product was obtained from 2,3-difluoro-4-(trifluoromethyl)benzyl alcohol (ABCR) and 1,4-benzodioxan-6-amine (Aldrich) as a crystalline yellow solid. MP 169-170 °C. MS (ESI, pos. ion) m/z: 386 (M+1).

Example 48



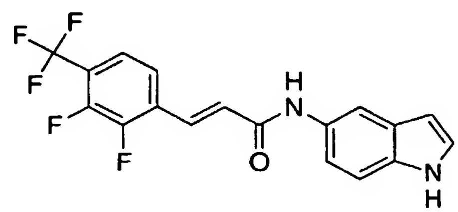
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[2,4-bis(trifluoromethyl)-phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 46**, steps (b)-(e), the title product was obtained from 2,4-bis(trifluoromethyl)benzyl alcohol (Avocado) and 1,4-benzodioxan-6-amine (Aldrich) as a crystalline yellow solid. MP 204-205 °C. MS (ESI, pos. ion) m/z: 418 (M+1).

Example 49



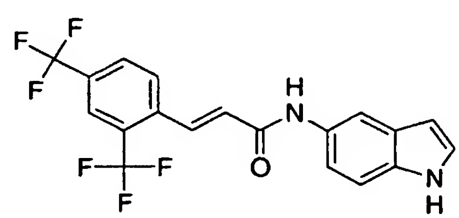
(2E)-3-[2-Fluoro-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 46**, steps (a)-(e), the title product was obtained from 2-fluoro-4-(trifluoromethyl)benzoic acid (ABCR) and 5-aminoindole (Aldrich) as a crystalline yellow solid. MP 203-205 °C. MS (ESI, pos. ion) m/z: 349 (M+1).

Example 50



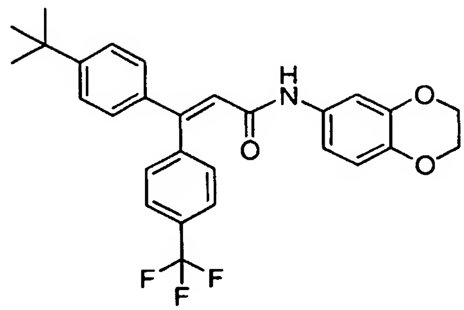
(2E)-3-[2,3-Difluoro-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 46**, steps (b)-(e), the title product was obtained from 2,3-difluoro-4-(trifluoromethyl)benzyl alcohol (ABCR) and 5-aminoindole (Aldrich) as a crystalline yellow solid. MP 220-222 °C. MS (ESI, pos. ion) m/z: 367 (M+1).

Example 51

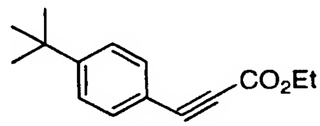


(2E)-3-[2,4-Bis(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 46**, steps (b)-(e), the title product was obtained from 2,4-bis(trifluoromethyl)benzyl alcohol (Avocado) and 5-aminoindole (Aldrich) as a crystalline yellow solid. MP 207-209 °C. MS (ESI, pos. ion) m/z: 399 (M+1).

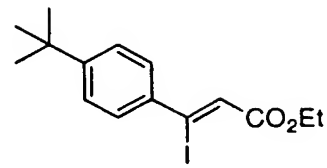
Example 52



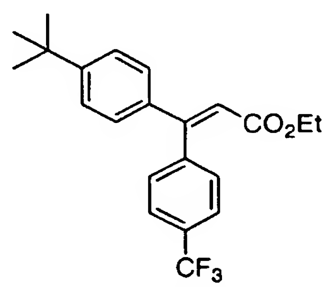
N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide.



(a). Ethyl 3-[4-(tert-butyl)phenyl]prop-2-ynoate. To a 1 L round-bottomed flask was added (4-*tert*-butyl)phenylacetylene (33.8 g, 214 mmol, GFS Chemicals) and anhydrous THF (220 mL). The solution was magnetically stirred, purged with N_2 and cooled to –78 °C, then *n*-butyllithium (136 mL, 2.5 M in hexanes, Aldrich) was added slowly. After the addition was complete, the mixture was gradually warmed to 0 °C and stirred magnetically for 30 min. The reaction mixture was cooled to –78 °C again and ethyl chloroformate (28.6 mL, 299.2 mmol, Aldrich) was added. After allowing to warm to 25 °C and stirring overnight, the reaction was quenched with 1:1 satd $NaHCO_3$:satd NH_4Cl (200 mL) and extracted with Et_2O (1000 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo to afford a yellow oil. Purification by silica gel chromatography (gradient: 0.5%-3% EtOAc/hexane) provided ethyl 3-[4-(*tert*-butyl)phenyl]prop-2-ynoate as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 231 (M+1).

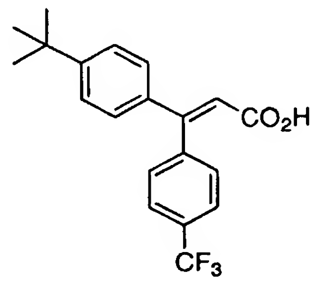


(b). Ethyl (2Z)-3-[4-(tert-butyl)phenyl]-3-iodoprop-2-enoate. According to the procedure of E. Piers et al., *Can. J. Chem.* **1994**, *72*, 1816, to a 150 mL round-bottomed flask equipped with a reflux condenser and magnetic stirring was added ethyl 3-[4-(*tert*-butyl)phenyl]prop-2-ynoate, **Example 52(a)**, (15 g, 65 mmol), sodium iodide (31 g, 209 mmol, Aldrich) and glacial acetic acid (48 mL, 830 mmol). The reaction mixture was purged with N_2 and the flask immersed in a pre-heated 115 °C oil bath. The reaction mixture was magnetically stirred at 115 °C for 4 h, then allowed to cool to 25 °C and treated with H_2O (200 mL). The aqueous phase was extracted with Et_2O (500 mL). The organic layer was washed with satd Na_2CO_3 until the evolution of CO_2 ceased, then washed with 1 M $Na_2S_2O_3$ (100 mL), satd NaCl, dried over Na_2SO_4, filtered, and concentrated in vacuo to provide ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enoate as a yellow oil. MS (ESI, pos. ion) *m/z*: 359 (M+1).



(c) Ethyl (2Z)-3-[4-(tert-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enoate. To a 100 mL round-bottomed flask equipped with a reflux condenser and magnetic stirring was added ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enoate, **Example 52(b)**, (0.75 g, 2.1 mmol), 4-trifluoromethylphenylboronic acid (0.60 g, 3.1 mmol, Aldrich), tetrakis(triphenylphosphine)palladium (0) (0.24 g, 0.21 mmol, Aldrich), toluene (10 mL), EtOH (2 mL), and 2 M aq. Na_2CO_3 (2 mL). The reaction mixture was magnetically stirred at 80 °C under N_2 overnight, allowed to cool to 25 °C and diluted with EtOAc (50 mL). The organic layer was separated, washed with H_2O, satd NaCl (50 mL), dried over Na_2SO_4,

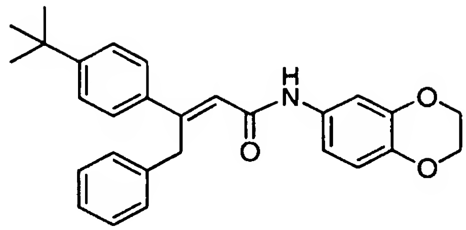
filtered and concentrated to afford a brown oil. Purification by silica gel chromatography (gradient: 1.5%-2% EtOAc/hexane) provided the title product as a white solid. MS (ESI, pos. ion) *m/z*: 377 (M+1).



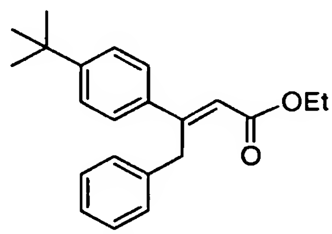
(d) (2Z)-3-[4-(tert-Butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enoic acid. To a 50 mL round-bottomed flask equipped with a reflux condenser was added ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enoate, **Example 52(c),** (0.74 g, 2.0 mmol), 1,4-dioxane (3 mL), KOH (0.66 g, 12 mmol) and H_2O (1.5 mL). The reaction mixture was heated and magnetically stirred under reflux overnight then diluted with H_2O (20 mL) and acidified with 1 N HCl. The aqueous mixture was extracted with CH_2Cl_2 (3 x 100 mL). The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo to provide the title product as a white solid. MS (ESI, pos. ion) *m/z*: 349 (M+1).

(e) N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2Z)-3-[4-(*tert*-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 52(d),** (0.15 g, 0.43 mmol) and 1,4-benzodioxan-6-amine (0.07 g, 0.43 mmol, Aldrich) provided, after purification by silica gel chromatography (gradient: 10%-18% EtOAc/hexane), the title product as a pale yellow solid. MP 150-151 °C. MS (ESI, pos. ion) *m/z*: 482 (M+1).

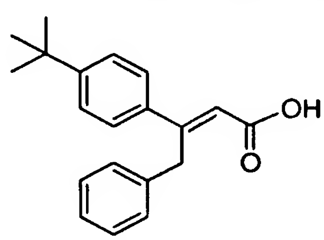
Example 53



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-phenylbut-2-enamide.



(a) Ethyl (2E)-3-[4-(tert-butyl)phenyl]-4-phenylbut-2-enoate. A solution of ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enoate, **Example 52(b),** (710 mg, 2.0 mmol) in anhydrous DMF (4 mL) was added dropwise to benzylzinc bromide (12 mL, 6.0 mmol, 0.5 M solution in THF, Aldrich) magnetically stirred under Ar at 0 °C in a round-bottomed flask. The mixture was treated with bis(acetonitrile)dichloropalladium (II) (78 mg, 0.30 mmol, Aldrich) in one portion. The reaction mixture was then magnetically stirred for 16 h at 25 °C, diluted with Et_2O (100 mL) and washed with 1N HCl (25 mL) and satd NaCl (25 mL). The organic phase was dried over $MgSO_4$, filtered and concentrated in vacuo and the residue purified by silica gel chromatography (49:1 hexane:EtOAc) to provide the title product as a colorless oil. MS (ESI, pos. ion) *m/z*: 323 (M+1).

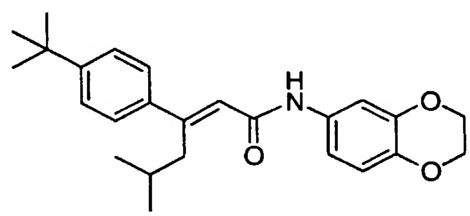


(b) (2E)-3-[4-(tert-Butyl)phenyl]-4-phenylbut-2-enoic acid. Ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-4-phenylbut-2-enoate, **Example 53(a),** (530 mg, 1.8 mmol) was treated with KOH (0.22 g, 4.0 mmol), H_2O (4 mL) and 1,4-dioxane (2 mL),

then magnetically stirred under reflux for 16 h. The reaction mixture was diluted with H_2O (50 mL), acidified with 1 N HCl and extracted with chloroform. The combined organic extract was washed with satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo. The resulting residue was crystallized from EtOAc and hexane to provide the title product as a white solid.

(c) (2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-phenylbut-2-enamide. Analogous to the procedure used to prepare **Example 1,** (2E)-3-[4-(*tert*-butyl)phenyl]-4-phenylbut-2-enoic acid, **Example 53(b),** (250 mg, 0.85 mmol) and 1,4-benzodioxan-6-amine (140 mg, 0.93 mmol, Aldrich) provided, after purification by silica gel chromatography (chloroform), the title product as off-white needles. MP 97–99 °C. MS (ESI, pos. ion) *m/z*: 428 (M+1).

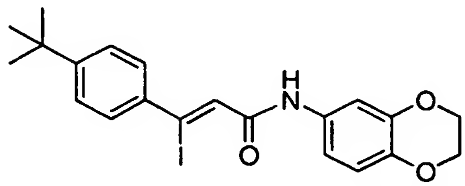
Example 54



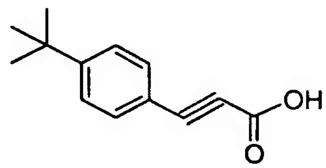
(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-5-methylhex-2-enamide.

Analogous to the procedure used to prepare **Example 53,** starting from 3-methylbutylzinc bromide (Aldrich), ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enoate, **Example 52(b),** and 1,4-benzodioxan-6-amine (Aldrich), the title product was obtained as an off-white solid. MP 123 °C. MS (ESI, pos. ion) *m/z*: 394 (M+1).

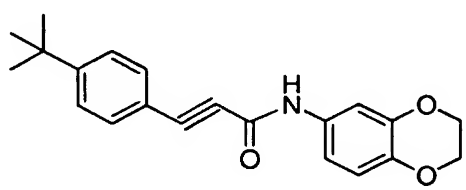
Example 55



N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-iodoprop-2-enamide.



(a) 3-[4-(tert-Butyl)phenyl]prop-2-ynoic acid. To a round-bottomed flask equipped with magnetic stirring and a reflux condenser was added a solution of ethyl 3-[4-(*tert*-butyl)phenyl]prop-2-ynoate, **Example 52(a)**, (4.6 g, 20 mmol) in 1,4-dioxane (5 mL). The solution was treated with H_2O (15 mL) and KOH (2.2 g, 40 mmol) then stirred and heated at reflux under Ar for 18 h. After allowing to cool to 25 °C, the mixture was diluted with H_2O (200 mL) and washed with Et_2O (50 mL). The aqueous phase was separated, acidified with 1 N HCl and extracted with chloroform. The chloroform extract was washed with satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo. Crystallization from EtOAc and hexane provided the title product as white needles. MS (ESI, pos. ion) *m/z*: 203 (M+1).

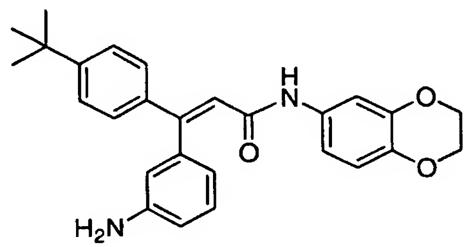


(b) N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-ynamide. Analogous to the procedure used to prepare **Example 1,** 3-[4-(*tert*-butyl)phenyl]prop-2-ynoic acid, **Example 55(a),** (404 mg, 2.0 mmol) and 1,4-benzodioxan-6-amine (330 mg, 2.2 mmol, Aldrich) provided the title product as a white solid. MP 199 °C. MS (ESI, pos. ion) *m/z*: 336 (M+1).

(c) N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-iodoprop-2-enamide. Analogous to the procedure described for the preparation

of **Example 52(b)**, N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(*tert*-butyl)phenyl]prop-2-ynamide, **Example 55(b),** (0.335 g, 1.0 mmol), sodium iodide (0.48 g, 3.2 mmol, Aldrich) and glacial acetic acid (0.73 mL) provided, after purification by silica gel chromatography (chloroform), the title product as yellow crystals. MP 164 °C. MS (ESI, pos. ion) *m/z*: 464 (M+1).

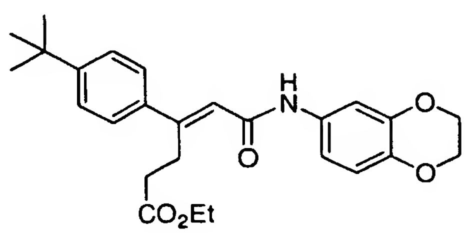
Example 56



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-(3-aminophenyl)-3-[4-(tert-butyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 52,** step (c), 3-aminophenylboronic acid (0.23 g, 1.5 mmol, Avocado) and N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enamide, **Example 55,** (0.46 g, 1.0 mmol) provided the title product as off-white crystals. MP 140 °C. MS (ESI, pos. ion) *m/z*: 429 (M+1).

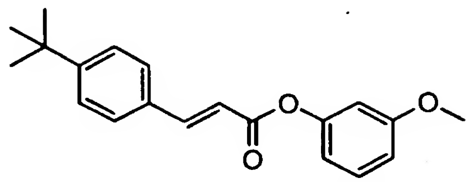
Example 57



Ethyl (4E)-5-(N-(2H,3H-benzo[e]1,4-dioxan-6-yl)carbamoyl)-4-[4-(tert-butyl)phenyl]pent-4-enoate.

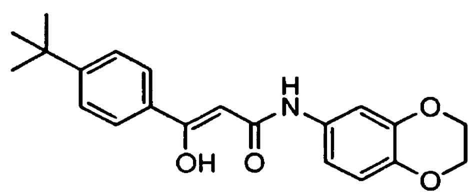
Analogously to the procedure used to prepare **Example 53,** step (a), 3-ethoxy-3-oxopropylzinc bromide (6.0 mL, 3.0 mmol, 0.5 M in THF, Aldrich) and N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enamide, **Example 55,** (0.46 g, 1.0 mmol) provided the title product as a pale yellow solid. MP 104–105 °C. MS (ESI, pos. ion) *m/z*: 438 (M+1).

Example 58

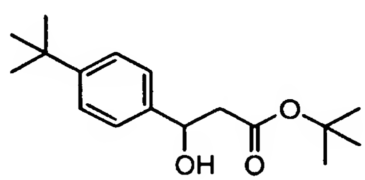


3-Methoxyphenyl (2E)-3-[4-(tert-butyl)phenyl]prop-2-enoate. To a 100 mL round-bottomed flask equipped with magnetic stirring was added 4-*tert*-butyl-*trans*-cinnamic acid (500 mg, 2.45 mmol, EMKA-Chemie), CH_2Cl_2 (10 mL), and DMF (10 uL) under N_2. The solution was treated dropwise with oxalyl chloride (4.0 mL, 8.0 mmol, 2.0 M in CH_2Cl_2, Aldrich) then stirred at 25 °C for 1 h. The reaction mixture was concentrated in vacuo and the residue treated with 3-methoxyphenol (269 uL, 2.45 mmol, Aldrich), THF (20 mL) and satd K_2CO_3 (15 mL). The reaction mixture was stirred at 25 °C overnight, then acidified to pH 4.5 with 1 N HCl. The mixture was extracted with EtOAc (2 × 30 mL), the combined organic extract was dried and concentrated in vacuo. Purification by silica gel chromatography (5:1 hexane:EtOAc) provided the title product as a white solid. MP 83 °C. MS (ESI, pos. ion) m/z: 311 (M+1).

Example 60

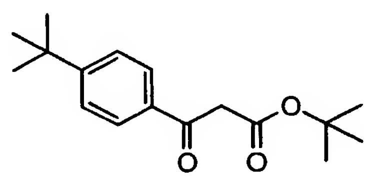


N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-hydroxyprop-2-enamide.



(a) **tert-Butyl 3-[4-(tert-butyl)phenyl]-3-hydroxypropanoate.** To a round-bottomed flask equipped with magnetic stirring was added *N,N*-diisopropylamine (10.4 mL, 74.0 mmol, Aldrich) and anhydrous THF (20 mL). The solution was stirred at –78 °C under N_2 and treated dropwise with *n*-butyllithium (30.0 mL,

75.0 mmol, 2.5 M in hexane, Aldrich). After stirring for 10 min at –78 °C, the reaction mixture was treated with *t*-butyl acetate (10.8 mL, 80.1 mmol, Aldrich). After stirring 30 min at –78 °C, the enolate was added via cannula to a solution of 4-*t*-butylbenzaldehyde (10.0 g, 61.6 mmol, Fluka) in anhydrous THF (100 mL), stirred under N_2 at –78 °C. The reaction mixture was allowed to warm to 0 °C with stirring over 3 h, then quenched with satd NH_4Cl and concentrated in vacuo to remove the THF. The resulting mixture was diluted with satd NH_4Cl (100 mL) and extracted with Et_2O (200 mL). The organic extract was washed with H_2O (100 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to provide the title product as a white solid. MS (ESI, pos. ion) *m/z*: 261 (M+1-H_2O).

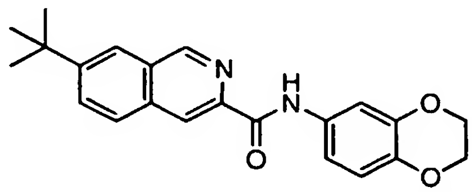


(b) **tert-butyl 3-[4-(tert-butyl)phenyl]-3-oxopropanoate**. *tert*-Butyl 3-[4-(*tert*-butyl)phenyl]-3-hydroxypropanoate, **Example 60(a),** (5.0 g, 18 mmol) was dissolved in CH_2Cl_2 (100 mL), magnetically stirred in a round-bottomed flask at 0 °C, and treated with pyridinium chlorochromate (5.8 g, 27 mmol, Aldrich) in portions. The reaction mixture was allowed to warm to 25 °C and stirred at that temperature for 5 h. The mixture was filtered through a pad of Celite, the filtercake washed with CH_2Cl_2 (3 x 100 mL) and the combined filtrate was concentrated in vacuo. Purification by silica gel chromatography (1:1 hexane:EtOAc) provided the title product as a dark oil. MS (ESI, pos. ion) *m/z*: 277 (M+1).

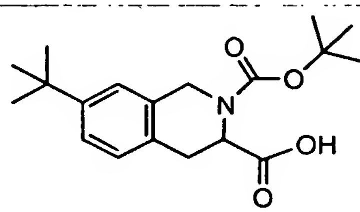
(c) **N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-hydroxyprop-2-enamide**. According to the procedure of Wiseman et al., *J. Org. Chem.* **1991**, *56*, 1713-1718, to a round-bottomed flask equipped with magnetic stirring and a reflux condenser was added *tert*-butyl 3-[4-(*tert*-butyl)phenyl]-3-oxopropanoate, **Example 60(b),** (640 mg, 2.3 mmol), 1,4-benzodioxan-6-amine (350 mg, 2.3 mmol, Aldrich) and anhydrous toluene (20 mL). The mixture was stirred and heated at 130 °C for 2 h. Upon allowing to cool to 25 °C, a precipitate

was observed. Hexane (20 mL) was added to the suspension and the precipitate collected by filtration, washed with hexane (20 mL) and dried in vacuo at 60 °C to provide the title product as a pale grey solid. MP 161 °C. MS (ESI, pos. ion) m/z: 354 (M+1).

Example 61



N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)[7-(tert-butyl)(3-isoquinolyl)]-carboxamide.

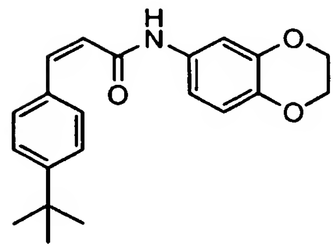


(a) **2-[(tert-Butyl)oxycarbonyl]-7-(tert-butyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid**. According to the procedure of D. Ma, et al., *Bioorg. Med. Chem. Lett.* **1998**, *8*(18), 2447-2450, to a 250 mL round-bottomed flask, equipped with magnetic stirring and reflux condenser, was added *N*-Boc-(*p*-*tert*-butyl)-*S*-phenylalanine (5.0 g, 15.6 mmol, Bachem), formaldehyde (50 mL, 37 wt. % in H_2O, Aldrich) and cond HCl (30 mL). The reaction mixture was stirred and heated at 90 °C for 4 h. The solvents were removed in vacuo to provide 3.6 g of a residue [MS (ESI, pos. ion) m/z: 234 (M+1)] which was dissolved in THF (140 mL) and treated with 5% aq. K_2CO_3 (140 mL) and di-*t*-butyl dicarbonate (4.8 g, 22 mmol, Aldrich). The reaction mixture was stirred at 25 °C overnight, then acidified to pH 5 with 1 N HCl. The mixture was extracted with EtOAc (300 mL), the organic phase washed with satd NaCl (100 mL) and H_2O (120 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (2:1 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) m/z: 334 (M+1).

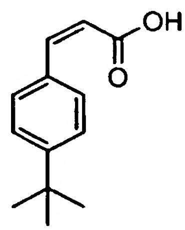
(b) N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)[7-(tert-butyl)(3-1,2,3,4-tetrahydroisoquinolyl)]carboxamide hydrochloride. To a 250 mL round-bottomed flask equipped with magnetic stirring was added 2-[(*tert*-butyl)oxycarbonyl]-7-(*tert*-butyl)-1,2,3,4-tetrahydroisoquinoline-3-carboxylic acid, **Example 61(a),** (1.5 g, 4.65 mmol), DMF (15 mL), 1,4-benzodioxan-6-amine (700 mg, 4.65 mmol, Aldrich), dimethylaminopropyl-3-ethylcarbodiimide hydrochloride (1.25 g, 6.5 mmol, Aldrich) and *N,N*-diisopropylethylamine (2.5 mL, 13.95 mmol, Aldrich). The reaction mixture was stirred at 25 °C overnight then concentrated in vacuo. The residue was dissolved in EtOAc (35 mL), washed with H_2O (2×15 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (3:1 hexane:EtOAc) provided a product [MS (ESI, pos. ion) m/z: 467 (M+1)] which was treated with 4.0 N HCl in 1,4 dioxane (10 mL, Aldrich) and stirred at 25 °C for 1 h. The solvent was removed in vacuo to provide the title product as the hydrochloride salt. MP 134 °C. MS (ESI, pos. ion) m/z: 367 (M+1).

(c) N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)[7-(tert-butyl)(3-isoquinolyl)]-carboxamide. Analogous to the procedure of E. D. Cox; T. J. Hagen; R. M. McKernan; J. M. Cook, *Med. Chem. Rest.* **1995**, 5(9), 710-718, N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)[7-(*tert*-butyl)(3-1,2,3,4-tetrahydroisoquinolyl)]carboxamide hydrochloride, **Example 61(b),** was suspended in EtOAc (55 mL), washed with 10% $NaHCO_3$ (20 mL) and H_2O (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. The resulting residue (80 mg, 0.22 mmol) was dissolved in toluene (10 mL) and treated with manganese dioxide (110 mg, 1.1 mmol). The reaction mixture was magnetically stirred at 70 °C under N_2 for 1.5 h, filtered through Celite and concentrated in vacuo. Purification by silica gel chromatography (8:1 hexane:EtOAc) provided the title product as a yellow solid. MP 154-157 °C. MS (ESI, pos. ion) m/z: 363 (M+1).

Example 63



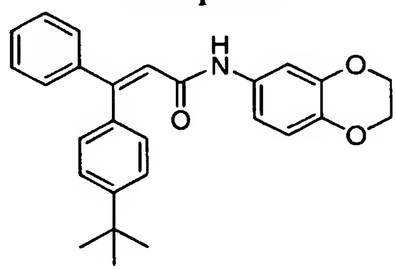
N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]prop-2-enamide.



(a) (2Z)-3-[4-(tert-Butyl)phenyl]prop-2-enoic acid. Potassium bis(trimethylsilyl)amide (6.1 mL, 3.05 mmol, 0.5 M in toluene, Aldrich) was added dropwise with stirring to a mixture of diphenylphosphonoacetic acid ethyl ester (0.98 g, 3.05 mmol, TCI-US) and 18-crown-6 (3.35 g, 12.7 mmol, Aldrich) in anhydrous THF (20 mL), magnetically stirred at -78 °C under Ar. The reaction mixture was stirred at -78 °C for 0.5 h then treated dropwise with a solution of 4-*tert*-butylbenzaldehyde (0.42 mL, 2.54 mmol, Aldrich) in anhydrous THF (5 mL). The mixture was stirred at -78 °C for 1 h, quenched with satd NH_4Cl (5 mL), warmed to 25 °C, diluted with H_2O (50 mL) and extracted with EtOAc (2 x 50 mL). The combined organic extracts were washed with satd NaCl, dried over $MgSO_4$, filtered and concentrated in vacuo to provide a brown viscous oil. [MS (ESI, pos. ion) *m/z*: 233 (M+1)] The oil (0.83 g) was dissolved in THF (5 mL) and MeOH (5 mL), magnetically stirred in a round-bottomed flask at 25 °C, and treated with 1 N LiOH (10 mL). The reaction mixture was stirred at 25 °C for 18 h, the organic solvents removed in vacuo, and the aqueous phase was washed with Et_2O, acidified with 10% citric acid and extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over $MgSO_4$, filtered and concentrated in vacuo to provide the title product as a white solid. MS (ESI, pos. ion) *m/z*: 205 (M+1).

(b) N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2Z)-3-[4-(*tert*-butyl)phenyl]prop-2-enoic acid, **Example 63(a)**, (0.46 g, 2.3 mmol) and 1,4-benzodioxan-6-amine (0.38 g, 2.58 mmol, Aldrich) provided the title product as a white solid. MP 114–116 °C. MS (ESI, pos. ion) *m/z*: 338 (M+1).

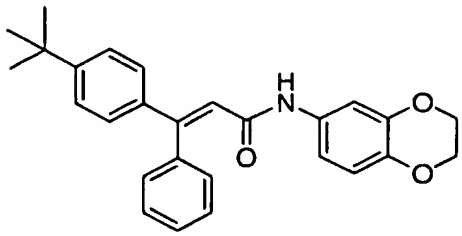
Example 64



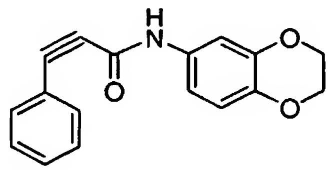
N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-phenylprop-2-enamide.

N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(*tert*-butyl)phenyl]prop-2-ynamide, **Example 55(b),** (0.34 g, 1.0 mmol) was dissolved in anhydrous EtOAc (50 mL) in a 100 mL round-bottomed flask equipped with reflux condenser and magnetic stirring under dry nitrogen atmosphere. To this solution was added iodobenzene (0.20 g, 1.0 mmol, Aldrich) and bis(dibenzylideneacetone)palladium (0.080 g, 0.14 mmol, Acros), followed by diethylamine (0.34 mL, 3.3 mmol, Aldrich) and formic acid (0.098 mL, 2.6 mmol, Aldrich). The reaction mixture was heated under reflux for 20 h, cooled to room temperature, washed with 1 N HCl (2 x 5 mL), 1 N NaOH (2 x 5 mL), satd NaCl (5 mL) and dried over Na_2SO_4. The organic solution was filtered and concentrated to afford a brown oil which was purified by silica gel chromatography (20 % EtOAc/hexane) to give the title compound as a pale yellow solid. MP 80-82 °C. MS (ESI, pos. ion) *m/z*: 414 (M+1).

Example 65



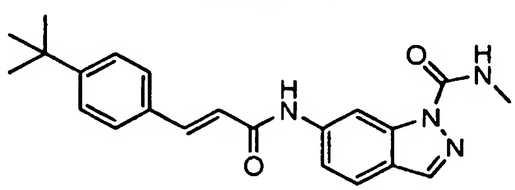
(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-3-phenylprop-2-enamide.



(a). N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-phenylprop-2-ynamide. Analogous to the procedure used to prepare **Example 1**, phenylpropiolic acid (5.8 g, 140 mmol, Aldrich) and 1,4-benzodioxan-6-amine (6.65 g, 44 mmol, Aldrich) provided, after recrystallization from EtOAc and hexane, the title compound as a white solid. MP 132 °C. MS (ESI, pos. ion) *m/z*: 280 (M+1).

(b). (2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-3-phenylprop-2-enamide. Analogous to the procedure used to prepare **Example 64**, 1-*tert*-butyl-4-iodobenzene (0.26 g, 1.0 mmol, Aldrich) and N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-phenylprop-2-ynamide, **Example 65(a),** (0.28 g, 1.0 mmol) provided, after recrystallization from EtOAc and hexane, the title compound as an off-white solid. MP 139 °C. MS (ESI, pos. ion) *m/z*: 414 (M+1).

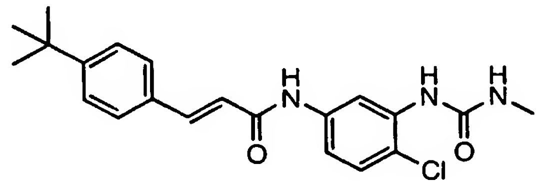
Example 66



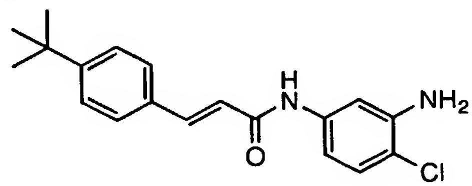
(2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(N-methylcarbamoyl)(1H-indazol-6-yl)]prop-2-enamide. To a round-bottomed flask, equipped with a magnetic stir bar, was added (2E)-N-(1H-indazol-6-yl)-3-[4-(*tert*-butyl)phenyl]prop-2-enamide, **Example 155**, (61 mg, 0.19 mmol), THF (8 mL) and isocyanatomethane (54 mg, 0.96 mmol, Carbolabs). The reaction mixture was stirred at room temperature for 8 h. The reaction mixture was diluted with EtOAc (10 mL), washed with water

(8 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (40:20:1 hexane:EtOAc:MeOH) provided the title product as an off-white solid. MP 208-209 °C. MS (ESI, pos. ion) m/z: 377 (M+1).

Example 67



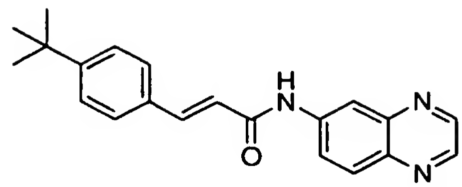
(2E)-3-[4-(tert-Butyl)phenyl]-N-{4-chloro-3-[(methylamino)carbonylamino]-phenyl}prop-2-enamide.



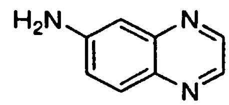
(a) (2E)-N-(3-Amino-4-chlorophenyl)-3-[4-(tert-butyl)phenyl]prop-2-enamide. To a round-bottomed flask equipped with a magnetic stir bar, was added (2E)-3-[4-(*tert*-butyl)phenyl]-N-(4-chloro-3-nitrophenyl)prop-2-enamide, **Example 156**, (250 mg, 0.69 mmol), EtOH (8 mL), indium (800 mg, 6.9 mmol, Aldrich) and satd NH_4Cl (10 mL). The reaction mixture was stirred at reflux for 5 h. The solvents were removed in vacuo, the residue was dissolved in EtOAc (20 mL), washed with water (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to yield the title product. MS (ESI, pos. ion) m/z: 329 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-{4-chloro-3-[(methylamino)-carbonylamino]phenyl}prop-2-enamide. According to the procedure used to prepare **Example 66**, (2E)-N-(3-amino-4-chlorophenyl)-3-[4-(*tert*-butyl)phenyl]prop-2-enamide, **Example 67(a)**, (90 mg, 0.27 mmol) and isocyanatomethane (156 mg, 2.7 mmol, Carbolabs) provided, after purification by silica gel chromatography (2:1 hexane:EtOAc), the title product as an off-white solid. MP 120-122 °C. MS (ESI, pos. ion) m/z: 386 (M+1).

Example 68



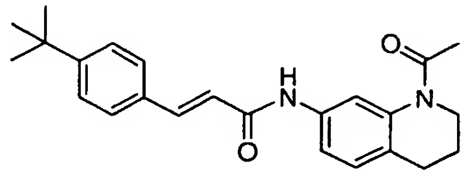
(2E)-3-[4-(tert-Butyl)phenyl]-N-quinoxalin-6-ylprop-2-enamide.



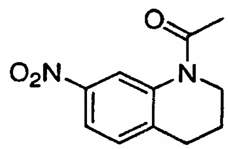
(a) Quinoxaline-6-ylamine. To a round-bottomed flask equipped with magnetic stirring was added 4-nitro-1,2-phenylenediamine (1.0 g, 6.5 mmol, Aldrich), acetonitrile (10 mL) and glyoxal (2.2 mL, 19 mmol, 40 wt. % in water, Aldrich). The reaction mixture was allowed to stir at 50 °C for 12 h, then concentrated in vacuo to yield 1.1 g crude 6-nitro-quinoxaline. The crude product was dissolved in methanol, treated with 10% Pd/C (10 mg, Aldrich) and stirred under H_2 (1 atm) at 25 °C overnight. The reaction mixture was filtered through Celite and the filtrate was concentrated in vacuo to provide the title product. MS (ESI, pos. ion) *m/z*: 146 (M+1).

(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-quinoxalin-6-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 2**, 4-*tert*-butyl-*trans*-cinnamic acid (100 mg, 0.40 mmol, EMKA-Chemie) and quinoxaline-6-ylamine, **Example 68(a),** (71 mg, 0.40 mmol) provided, after purification by silica gel chromatography (1:2 hexane:EtOAc), the title product as a yellow solid. MP 229-230 °C. MS (ESI, pos. ion) *m/z*: 332 (M+1).

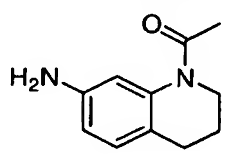
Example 69



(2E)-N-(1-acetyl(7-1,2,3,4-tetrahydroquinolyl))-3-[4-(tert-butyl)phenyl]prop-2-enamide.



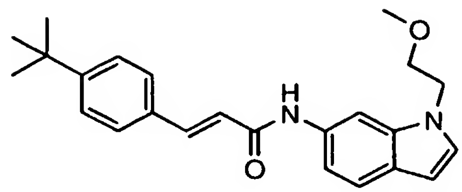
(a) 1-Acetyl-7-nitro-1,2,3,4-tetrahydroquinoline. A mixture of 7-nitro-1,2,3,4-tetrahydroquinoline, **Example 19(a),** (0.36 g , 2.0 mmol) and acetic anhydride (3.5 mL, 37 mmol, Aldrich) in a 15 mL round-bottomed flask, was heated at reflux for 1.5 h. The reaction mixture was concentrated in vacuo and the residue was partitioned between EtOAc and 30% ammonium hydroxide. The aqueous layer was extracted with EtOAc (10 mL) and the combined organic layers were dried over Na_2SO_4, filtered and concentrated in vacuo to give the title compound as a yellow solid. MS (ESI, pos. ion) *m/z*: 221 (M+1).



(b) 1-Acetyl-7-amino-1,2,3,4-tetrahydroquinoline. Analogous to the procedure used to prepare **Example 3**, step (a), 1-acetyl-7-nitro-1,2,3,4-tetrahydroquinoline, **Example 69(a),** (0.44 g, 2.0 mmol) was converted to the title product. MS (ESI, pos. ion) *m/z*: 191 (M+1).

(c) (2E)-N-(1-acetyl(7-1,2,3,4-tetrahydroquinolyl))-3-[4-(tert-butyl)phenyl]prop-2-enamide. According to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (0.41 g, 2.0 mmol, EMKA Chemie) and 1-acetyl-7-amino-1,2,3,4-tetrahydroquinoline, **Example 69(b),** (370 mg, 2.0 mmol) provided, after purification by silica gel chromatography (1:1 hexane:EtOAc), the title compound as an amorphous white solid. MS (ESI, pos. ion) *m/z*: 377 (M+1).

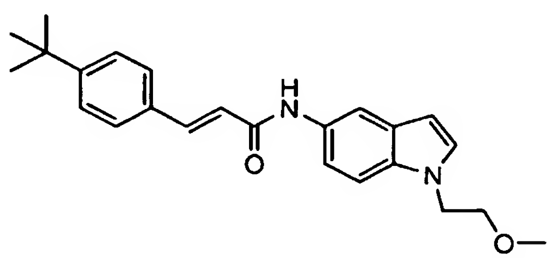
Example 70



(2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-methoxyethyl)indol-6-yl]prop-2-enamide.

To a round-bottomed flask was added, (2E)-3-[4-(*tert*-butyl)phenyl]-N-indol-6-ylprop-2-enamide, **Example 189,** (320 mg, 1.0 mmol) and anhydrous DMF (20 mL). The solution was stirred magnetically and treated with sodium hydride (0.10 g, 2.5 mmol, 60% dispersion in mineral oil, Aldrich) followed by 2-bromoethyl methyl ether (140 mg, 1.0 mmol, Aldrich). Stirring was continued at 25 °C for 2 h, then the reaction mixture was quenched by the addition of water (50 mL) and extracted with EtOAc. The organic extract was concentrated in vacuo. Purification by silica gel chromatography (60:40 hexane:EtOAc) provided the title compound as a yellow solid. MP 133 °C. MS (ESI, pos. ion) *m/z*: 377 (M+1).

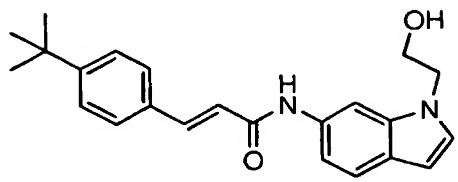
Example 71



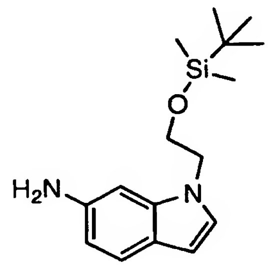
(2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-methoxyethyl)indol-5-yl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 70**, 2-bromoethyl methyl ether (140 mg, 1.0 mmol, Aldrich) and (2E)-3-[4-(*tert*-butyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 161,** (320 mg, .01 mmol) provided, after purification by silica gel chromatography (65:35 hexane:EtOAc), the title compound as a pale yellow solid. MP 138 °C. MS (ESI, pos. ion) *m/z*: 377 (M+1).

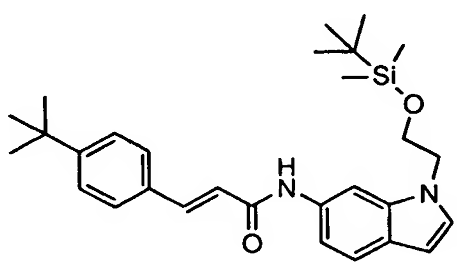
Example 72



(2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-6-yl]prop-2-enamide.



(a) 1-[2-(1,1,2,2-Tetramethyl-1-silapropoxy)ethyl]indole-6-ylamine. Analogous to the procedure used to prepare **Example 33,** step (a), 6-nitroindole (0.49 g, 3.0 mmol, Aldrich) and (2-bromoethoxy)-*tert*-butyldimethylsilane (0.72 g, 3.0 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 291 (M+1).

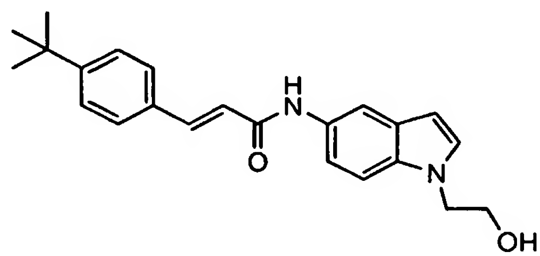


(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-6-yl}prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and 1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indole-6-ylamine, **Example 72(a),** (290 mg, 1.0 mmol) provided the title product. MS (ESI, pos. ion) *m/z*: 477 (M+1).

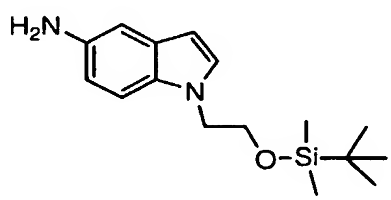
(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-6-yl]prop-2-enamide. (2E)-3-[4-(*tert*-Butyl)phenyl]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-6-yl}prop-2-enamide, **Example 72(b),** (420 mg,

0.88 mmol) was transferred to a round-bottomed flask and treated with tetrabutylammonium fluoride (2.0 mL, 2.0 mmol, 1.0 M in THF, Aldrich) under N_2. The reaction mixture was magnetically stirred at 25 °C for 2 h. The reaction mixture was diluted with water (25 mL) and extracted with EtOAc. The organic extract was concentrated in vacuo. Purification by silica gel chromatography (30:70 hexane:EtOAc) provided the title compound as a yellow solid. MP 178 °C. MS (ESI, pos. ion) *m/z*: 363 (M+1).

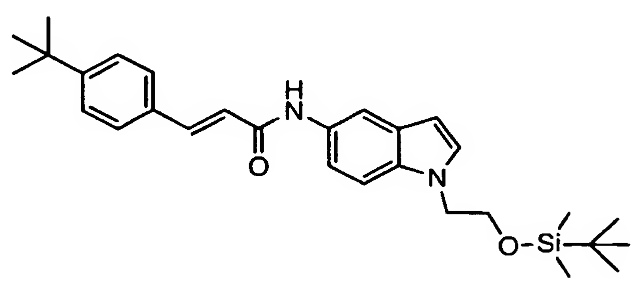
Example 73



(2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide.



(a) 1-[2-(1,1,2,2-Tetramethyl-1-silapropoxy)ethyl]indole-5-ylamine. According to the procedure used to prepare **Example 33,** step (a), 5-nitroindole (0.49 g, 3.0 mmol, Aldrich) and (2-bromoethoxy)-*tert*-butyldimethylsilane (0.72 g, 3.0 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 291 (M+1).

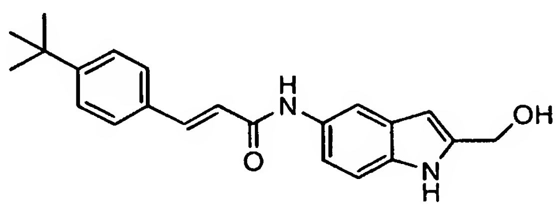


(b) (2E)-3-[4-(tert-Butyl)phenyl]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-5-yl}prop-2-enamide. According to the procedure used

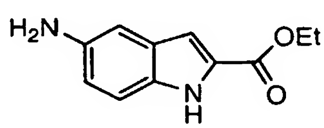
to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (100 mg, 0.50 mmol, EMKA-Chemie) and 1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indole-5-ylamine, **Example 73(a)**, (145 mg, 0.50 mmol) provided the title product. MS (ESI, pos. ion) *m/z*: 477 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide. According to the procedure used to prepare **Example 72**, step (c), (2E)-3-[4-(*tert*-butyl)phenyl]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-5-yl}prop-2-enamide, **Example 73(b)**, (130 mg, 0.27 mmol) and tetrabutylammonium fluoride(1.0 mL, 1.0 mmol, 1.0 M in THF, Aldrich) provided, after purification by silica gel chromatography (30:70 hexane:EtOAc), the title compound as a pale yellow solid. MP 182 °C. MS (ESI, pos. ion) *m/z*: 363 (M+1).

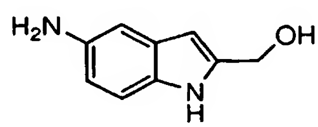
Example 74



(2E)-3-[4-(tert-Butyl)phenyl]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide.



(a) Ethyl 5-aminoindole-2-carboxylate. Analogous to the procedure used to prepare **Example 3**, step (a), ethyl 5-nitroindole-2-carboxylate (2.3 g, 9.9 mmol, Acros) provided the title product. MS (ESI, pos. ion) *m/z*: 205 (M+1).

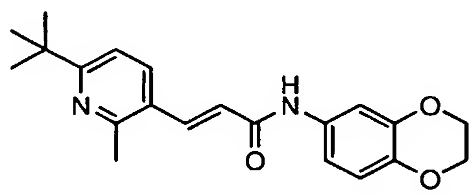


(b) (5-Aminoindol-2-yl)methan-1-ol. Ethyl 5-aminoindole-2-carboxylate, **Example 74(a)**, (1.5 g, 7.3 mmol) was transferred to a round-bottomed flask and treated with lithium aluminum hydride (10 mL, 10 mmol, 1.0 M in THF, Aldrich) under N_2. The reaction mixture was magnetically stirred at 25 °C for 1 h, then

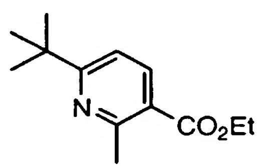
quenched by the dropwise addition of H_2O (0.5 mL) followed by 20% aq. KOH (30 mL). The suspension was filtered and the aqueous phase extracted with EtOAc. The organic extract was concentrated in vacuo. Purification of the crude product by silica gel chromatography (20:80 hexane:EtOAc) provided the title product. MS (ESI, pos. ion) *m/z*: 163 (M+1).

(c) (2E)-3-[4-(tert-Butyl)phenyl]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (200 mg, 1.0 mmol, EMKA-Chemie) and (5-aminoindol-2-yl)methan-1-ol, **Example 74(b)**, (160 mg, 1.0 mmol) provided, after purification by silica gel chromatography (40:60 hexane:EtOAc), the title product as a pale tan amorphous solid. MS (ESI, pos. ion) *m/z*: 349 (M+1).

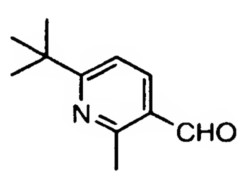
Example 75



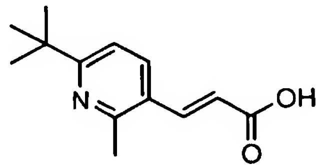
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]prop-2-enamide.



(a) Ethyl 6-(tert-butyl)-2-methylpyridine-3-carboxylate. Analogous to the procedure used to prepare **Example 44**, step (a), ethyl 2-methylnicotinate (8.3 g, 50 mmol, Aldrich), trimethylacetic acid (26 g, 250 mmol, Aldrich), silver nitrate (1.7 g, 10 mmol, Aldrich), 10% aq. sulfuric acid (50 mL) and ammonium persulfate (23 g, 100 mmol, Aldrich) provided, after purification by silica gel chromatography (80:20 hexane:EtOAc), the title product. MS (ESI, pos. ion) *m/z*: 222 (M+1).



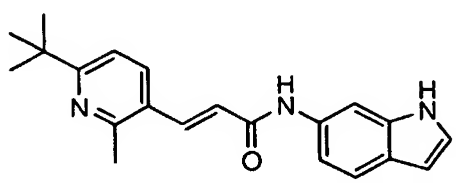
(b) 6-(tert-Butyl)-2-methylpyridine-3-carbaldehyde. Analogous to the procedure used to prepare **Example 43**, step (b), ethyl 6-(*tert*-butyl)-2-methylpyridine-3-carboxylate, **Example 75(a),** (5.2 g, 23 mmol) provided the title product. MS (ESI, pos. ion) *m/z*: 178 (M+1).



(c) (2E)-3-[6-(tert-Butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid. Analogous to the procedure used to prepare **Example 40**, step (a), 6-(*tert*-butyl)-2-methylpyridine-3-carbaldehyde, **Example 75(b),** (3.0 g, 17 mmol) and triethyl phosphonoacetate (4.0 g, 18 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 220 (M+1).

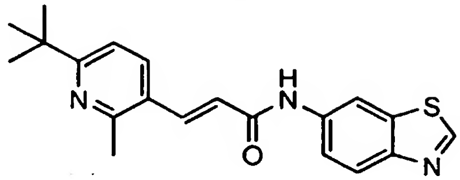
(d) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid, **Example 75(c),** (110 mg, 0.50 mmol) and 1,4-benzodioxan-6-amine (76 mg, 0.50 mmol, Aldrich) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow amorphous solid. MS (ESI, pos. ion) *m/z*: 353 (M+1).

Example 76



(2E)-3-[6-(tert-Butyl)-2-methyl(3-pyridyl)]-N-indol-6-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid, **Example 75(c),** (220 mg, 1.0 mmol) and 6-aminoindole (130 mg, 1.0 mmol, Lancaster) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow solid. MP 182 °C. MS (ESI, pos. ion) *m/z*: 334 (M+1).

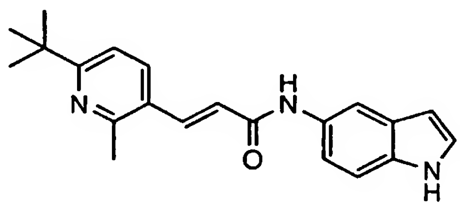
Example 77



(2E)-N-Benzothiazol-6-yl-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid, **Example 75(c)**, (220 mg, 1.0 mmol) and 6-aminobenzothiazole (150 mg, 1.0 mmol, Lancaster) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a pale yellow amorphous solid. MS (ESI, pos. ion) *m/z*: 352 (M+1).

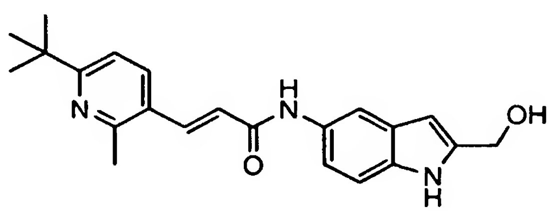
Example 78



(2E)-3-[6-(tert-Butyl)-2-methyl(3-pyridyl)]-N-indol-5-ylprop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid, **Example 75(c)**, (0.88 g, 4.0 mmol) and 5-aminoindole (0.53 g, 4.0 mmol, Lancaster) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow amorphous solid. MS (ESI, pos. ion) *m/z*: 334 (M+1).

Example 79

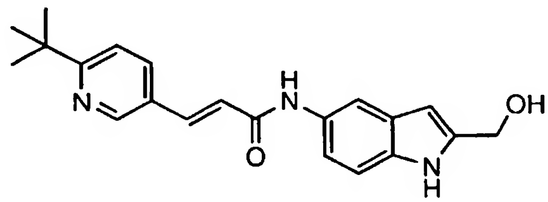


(2E)-3-[6-(tert-Butyl)-2-methyl(3-pyridyl)]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)-2-methyl(3-pyridyl)]prop-2-enoic acid, **Example 75(c)**, (110 mg, 0.50 mmol) and

(5-aminoindol-2-yl)methan-1-ol, **Example 74(b),** (81, 0.50 mmol) provided, after purification by silica gel chromatography (25:75 hexane:EtOAc), the title compound as a pale yellow solid. MP 213 °C. MS (ESI, pos. ion) *m/z*: 364 (M+1).

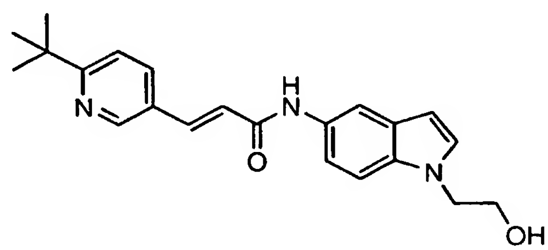
Example 80



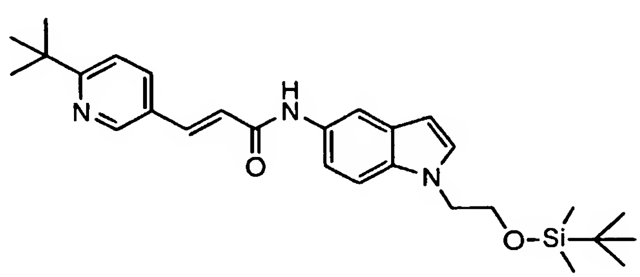
(2E)-3-[6-(tert-Butyl)(3-pyridyl)]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1,** (2E)-3-[6-(*tert*-butyl)(3-pyridyl)]prop-2-enoic acid, **Example 44(b),** (41 mg, 0.20 mmol) and (5-aminoindol-2-yl)methan-1-ol, **Example 74(b),** (32 mg, 0.20 mmol) provided, after purification by silica gel chromatography (20:80 hexane:EtOAc), the title compound as a yellow amorphous solid. MS (ESI, pos. ion) *m/z*: 350 (M+1).

Example 81



(2E)-3-[6-(tert-Butyl)(3-pyridyl)]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide.

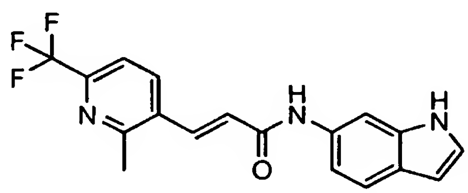


(a) (2E)-3-[6-(tert-butyl)(3-pyridyl)]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-5-yl}prop-2-enamide. Analogous to the procedure used

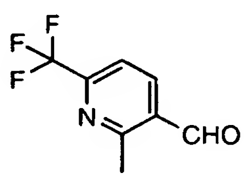
to prepare **Example 1**, (2E)-3-[6-(*tert*-butyl)(3-pyridyl)]prop-2-enoic acid, **Example 44(b),** (41 mg, 0.20 mmol) and 1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indole-5-ylamine, **Example 73(a)**, (60 mg, 0.20 mmol) provided the title product. MS (ESI, pos. ion) *m/z*: 478 (M+1).

(b) (2E)-3-[6-(tert-Butyl)(3-pyridyl)]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide. Analogous to the procedure used to prepare **Example 72**, step (c), (2E)-3-[6-(*tert*-butyl)(3-pyridyl)]-N-{1-[2-(1,1,2,2-tetramethyl-1-silapropoxy)ethyl]indol-5-yl}prop-2-enamide, **Example 81(a)**, (75 mg, 0.16 mmol) and tetrabutylammonium fluoride (0.50 mL, 0.50 mmol, 1.0 M in THF, Aldrich) provided, after purification by silica gel chromatography (20:80 hexane:EtOAc), the title compound as a yellow amorphous solid. MS (ESI, pos. ion) *m/z*: 364 (M+1).

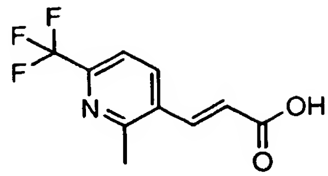
Example 82



(2E)-N-Indol-6-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide.



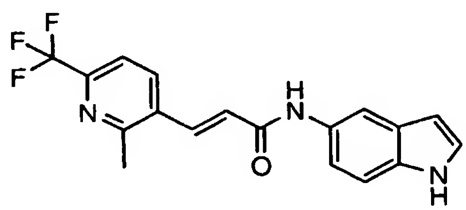
(a) 2-Methyl-6-(trifluoromethyl)pyridine-3-carbaldehyde. Analogous to the procedure used to prepare **Example 43**, step (b), 2-methyl-6-(trifluoromethyl)pyridine-3-carboxylic acid (5.0 g, 24 mmol, Oakwood) provided the title product. MS (ESI, pos. ion) *m/z*: 190 (M+1).



(b) (2E)-3-[2-Methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid. Analogous to the procedure used to prepare **Example 40**, step (a), 2-methyl-6-(trifluoromethyl)pyridine-3-carbaldehyde , **Example 82(a),** (3.7 g, 20 mmol) and triethyl phosphonoacetate (4.5 g, 20 mmol, Aldrich) provided the title product. MS (ESI, pos. ion) *m/z*: 232 (M+1).

(c) (2E)-N-Indol-6-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid, **Example 82(b),** (58 mg, 0.25 mmol) and 6-aminoindole (33 mg, 0.25 mmol, Lancaster) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow solid. MP 223 °C. MS (ESI, pos. ion) *m/z*: 346 (M+1).

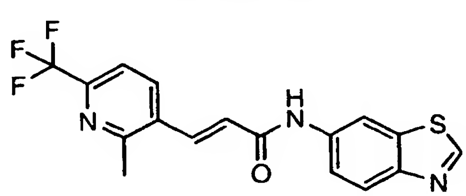
Example 83



(2E)-N-Indol-5-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid, **Example 82(b),** (120 mg, 0.50 mmol) and 5-aminoindole (66 mg, 0.50 mmol, Aldrich) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow solid. MP 231 °C. MS (ESI, pos. ion) *m/z*: 346 (M+1).

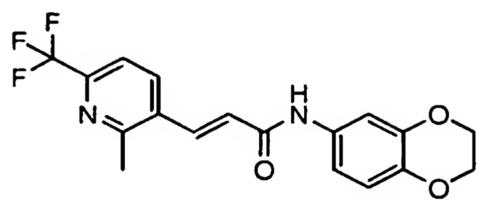
Example 84



(2E)-N-Benzothiazol-6-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid, **Example 82(b)**, (120 mg, 0.50 mmol) and 6-aminobenzothiazole (75 mg, 0.50 mmol, Lancaster) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a white solid. MP 196 °C. MS (ESI, pos. ion) *m/z*: 364 (M+1).

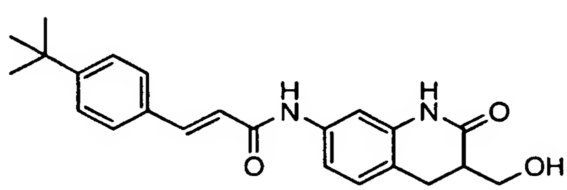
Example 85



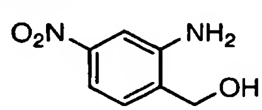
(2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[2-methyl-6-(trifluoromethyl)-(3-pyridyl)]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid, **Example 82(b)**, (120 mg, 0.50 mmol) and 1,4-benzodioxan-6-amine (76 mg, 0.50 mmol, Aldrich) provided, after purification by silica gel chromatography (55:45 hexane:EtOAc), the title compound as a yellow solid. MP 186 °C. MS (ESI, pos. ion) *m/z*: 365 (M+1).

Example 86

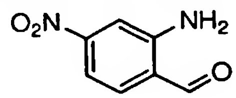


(2E)-3-[4-(tert-butyl)phenyl]-N-[3-(hydroxymethyl)-2-oxo(7-1,3,4-trihydroquinolyl)]prop-2-enamide.

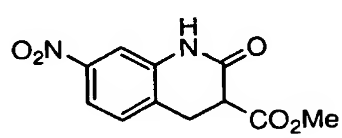


(a) (2-Amino-4-nitrophenyl)methan-1-ol. To a solution of 4-nitroanthranilic acid (910 mg, 5.0 mmol, Aldrich) in THF (15 mL), magnetically stirred at 0 °C, was added borane-tetrahydrofuran complex (15 mL, 15 mmol, 1.0 M in THF,

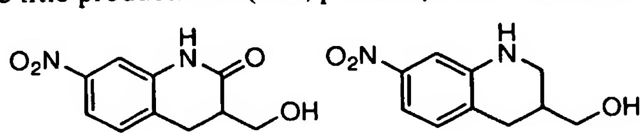
Aldrich) dropwise. The reaction mixture was heated to reflux overnight. The mixture was then cooled to 0 °C and treated dropwise with MeOH (5 mL) followed by 1 N NaOH (30 mL). After stirring for 30 min at room temperature, the mixture was extracted with EtOAc (2 x 50 mL). The combined organic phases were washed with satd NaCl (20 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (50% EtOAc/hexane) followed by recrystallization from EtOAc/hexane provided the title product. MS (ESI, pos. ion) m/z: 169 (M+1).



(b) 2-Amino-4-nitrobenzaldehyde. A mixture of 2-amino-4-nitrophenyl)methan-1-ol, **Example 86(a),** (336 mg, 2.0 mmol) and MnO_2 (3.48 g, 40.0 mmol, Aldrich) in CH_2Cl_2/hexane (1:1, 10 mL) was stirred at room temperature for 1 h. The suspension was filtered and washed with CH_2Cl_2. The filtrate was concentrated in vacuo to give the crude product. MS (ESI, pos. ion) m/z: 167 (M+1).

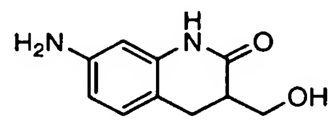


(c) Methyl 7-nitro-2-oxo-1,3,4-trihydroquinoline-3-carboxylate. A mixture of 2-amino-4-nitrobenzaldehyde, **Example 86(b),** (1.66 g, 10.0 mmol), dimethyl malonate (1.37 mL, 12.0 mmol, Aldrich), copper (II) acetate (100 mg, 0.5 mmol, Aldrich) and potassium acetate (99 mg, 1.0 mmol, Bayer) in acetic acid (20 mL) was stirred at 110 °C for 48 h. Most of the solvent was removed in vacuo and the resulting precipitate was collected by filtration, washed with EtOAc and dried in vacuo to give the title product. MS (ESI, pos. ion) m/z: 248 (M+1)



(d) 3-(Hydroxymethyl)-7-nitro-1,3,4-trihydroquinolin-2-one and (7-nitro-3-1,2,3,4-tetrahydroquinolyl)methan-1-ol. To a solution of methyl 7-nitro-2-oxo-1,3,4-trihydroquinoline-3-carboxylate, **Example 86(c),** (1.23 g, 5.0 mmol) in THF

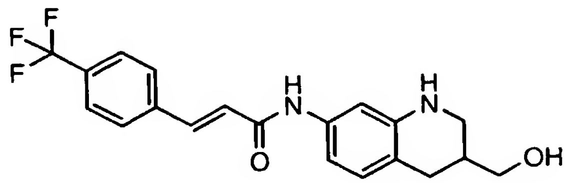
(50 mL) was added $LiBH_4$ (12.5 mL, 25.0 mmol, 2.0 M in THF, Aldrich). The reaction mixture was stirred at 40 °C for 18 h, then quenched by the careful addition of satd NH_4Cl (20 mL). The mixture was stirred at room temperature for 30 min, then extracted with EtOAc (2 x 50 mL). The combined organic phases were washed with satd NaCl (10 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (50% EtOAc/CH_2Cl_2) provided 3-(hydroxymethyl)-7-nitro-1,3,4-trihydroquinolin-2-one [MS (ESI, pos. ion) m/z: 223 (M+1)] and (7-nitro-3-1,2,3,4-tetrahydroquinolyl)methan-1-ol [MS (ESI, pos. ion) m/z: 209 (M+1)].



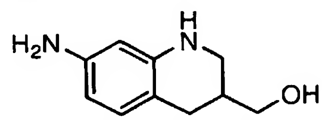
(e) 7 -Amino-3-(hydroxymethyl)-1,3,4-trihydroquinolin-2-one. Analogous to the procedure used to prepare **Example 3**, step (a), 3-(hydroxymethyl)-7-nitro-1,3,4-trihydroquinolin-2-one, **Example 86(d)**, (66 mg, 0.30 mmol) provided, after purification by silica gel chromatography (10% MeOH/CH_2Cl_2), the title compound. MS (ESI, pos. ion) m/z: 193 (M+1).

(f) (2E)-3-[4-(tert-Butyl)phenyl]-N-[3-(hydroxymethyl)-2-oxo(7-1,3,4-trihydroquinolyl)]prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, 4-*tert*-butyl-*trans*-cinnamic acid (67 mg, 0.33 mmol, EMKA-Chemie) and 7 -amino-3-(hydroxymethyl)-1,3,4-trihydroquinolin-2-one, **Example 86(e)**, (52 mg, 0.27 mmol) provided, after purification by silica gel chromatography (10% MeOH/EtOAc), the title compound as a pale yellow solid. MP 201-203 °C. MS (ESI, pos. ion) m/z: 379 (M+1).

Example 87



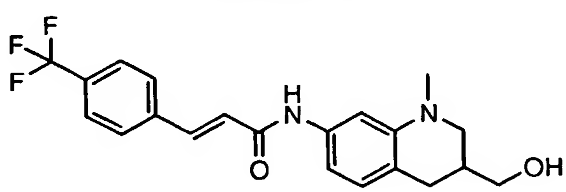
(2E)-N-[3-(Hydroxymethyl)(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide.



(a) (7-Amino-3-1,2,3,4-tetrahydroquinolyl)methan-1-ol. Analogous to the procedure used to prepare **Example 3,** step (a), (7-nitro-3-1,2,3,4-tetrahydroquinolyl)methan-1-ol, **Example 86(d),** (140 mg, 0.68 mmol) provided, after purification by silica gel chromatography (10% MeOH/CH_2Cl_2), the title compound. MS (ESI, pos. ion) m/z: 179 (M+1).

(b) (2E)-N-[3-(Hydroxymethyl)(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide. Analogous to the procedure used to prepare **Example 1,** *trans*-4-(trifluoromethyl)cinnamic acid (120 mg, 0.55 mmol, Aldrich) and (7-amino-3-1,2,3,4-tetrahydroquinolyl)methan-1-ol, **Example 87(a),** (98 mg, 0.55 mmol) provided, after purification by silica gel chromatography (10% MeOH/EtOAc), the title compound as a pale yellow solid. MP 176-179 °C. MS (ESI, pos. ion) m/z: 377 (M+1).

Example 88

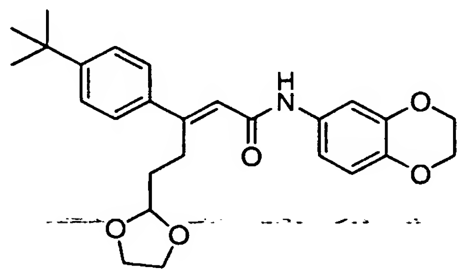


(2E)-N-[3-(hydroxymethyl)-1-methyl(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide.

A mixture of (2E)-N-[3-(hydroxymethyl)(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide, **Example 87,** (75 mg, 0.20 mmol), iodomethane (0.014 mL, 0.22 mmol, Aldrich) and $NaHCO_3$ (84 mg, 1.0 mmol) in

DMF (1.0 mL, Aldrich) was stirred for 4 h at room temperature. Water (5 mL) was added and the mixture was extracted with EtOAc (2 x 20 mL). The combined organic phases were washed with water (5 mL), satd NaCl (5mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (60% EtOAc/CH_2Cl_2) provided the title product as a white solid. MP 167-169 °C. MS (ESI, pos. ion) m/z: 391 (M+1).

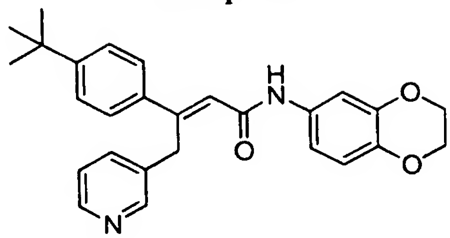
Example 89



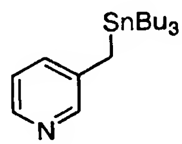
(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-5-(1,3-dioxolan-2-yl)pent-2-enamide.

Analogous to the procedure used to prepare **Example 53(a),** (1,3-dioxolan-2-ylethyl)zinc bromide (3.0 mL, 1.5 mmol, 0.5 M THF solution, Rieke) and N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enamide, **Example 55,** (0.23 g, 0.50 mmol) provided, after purification by silica gel chromatography (gradient: 30%-35% EtOAc/hexane), the title product as an amorphous white solid. MS (ESI, pos. ion) *m/z*: 438 (M+1).

Example 90



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-(3-pyridyl)but-2-enamide.

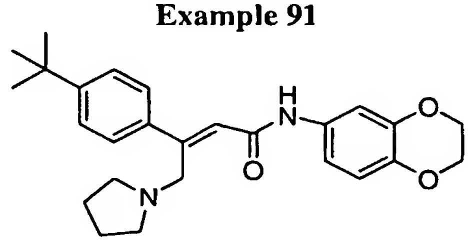


(a). 3-(Tributylstannanylmethyl)pyridine. Analogous to the procedure of Kaiser, E. M. and Petty, J. D. *Synthesis* **1975**, 705-706, to a 50 mL round-bottomed flask equipped with magnetic stirring was added lithium diisopropylamide (5.2 mL, 10 mmol, 2.0 M in heptane/THF/ethylbenzene, Aldrich) at 0 °C under nitrogen, followed by hexamethylphosphoramide (1.8 mL, 10 mmol, Aldrich). The mixture was stirred for 15 min, then treated with a solution of 3-picoline (1.0 mL, 10 mmol, Aldrich) in THF (4 mL) over 5 min. The reaction mixture was stirred for 30 min, then a solution of tributyltin chloride (2.8 mL, 10 mmol, Aldrich) in THF (6 mL) was added. The resulting solution was gradually warmed to room temperature and concentrated in vacuo. Purification by silica gel chromatography (gradient: 2%-5% EtOAc/hexane) provided the title product as a colorless oil. MS (ESI, pos. ion) *m/z*: 382 (M+1).

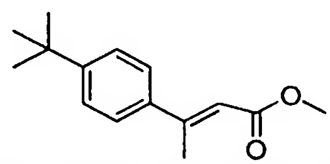
(b) (2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-(3-pyridyl)but-2-enamide. To a 50 mL round-bottomed flask, equipped with magnetic stirring, was added 3-(tributylstannanylmethyl)pyridine, **Example 90(a),** (0.37 g, 0.97 mmol), N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enamide, **Example 55,** (0.30 g, 0.65 mmol), 1-methyl-2-pyrrolidinone (2.5 mL, Aldrich), and tetrakis(triphenylphosphine)-palladium (0) (75 mg, 0.06 mmol, Aldrich). The reaction mixture was stirred at 110 °C overnight, then diluted with EtOAc (100 mL), washed with satd $NaHCO_3$, water and satd NaCl. The organic phase was dried over Na_2SO_4, filtered and

concentrated in vacuo. Purification by silica gel chromatography (25%-45% EtOAc/hexane) was followed by reverse phase preparative HPLC (CH_3CN/H_2O with 0.1%TFA). The fractions containing desired product were neutralized with $NaHCO_3$. The mixture was extracted with CH_2Cl_2 and the organic phase concentrated in vacuo to provide the title product as an amorphous white solid. MS (ESI, pos. ion) *m/z*: 429 (M+1).

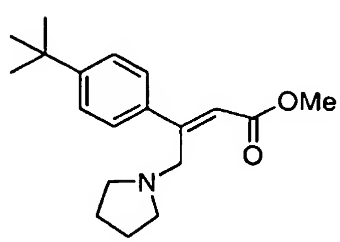
Example 91



N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-4-pyrrolidinylbut-2-enamide.



(a). Methyl (2E)-3-[4-(tert-butyl)phenyl]but-2-enoate. To a 100 mL round-bottomed flask purged with N_2 was added 1-bromo-4-*tert*-butylbenzene (2.34 g, 11.0 mmol, Aldrich), methyl crotonate (1.08 mL, 10 mmol, Aldrich), *N*-methyldicyclohexylamine (3.31 mL, 15 mmol, Aldrich), palladium acetate (0.045 g, 0.20 mmol, Aldrich), tetraethylammonium chloride (1.66 g, 10.0 mmol, Fluka), and *N,N*-dimethylacetamide (40 mL, Aldrich). The reaction mixture was magnetically stirred at 100 °C overnight, then allowed to cool to 25 °C, diluted with Et_2O, and filtered through Celite. The solution was washed with H_2O (3 x), dried over $MgSO_4$, filtered, and concentrated in vacuo. Purification by silica gel chromatography (gradient: 0.5%-3% dichloromethane in hexane) provided the title product as a colorless oil. MS (ESI, pos. ion) *m/z*: 233 (M+1).

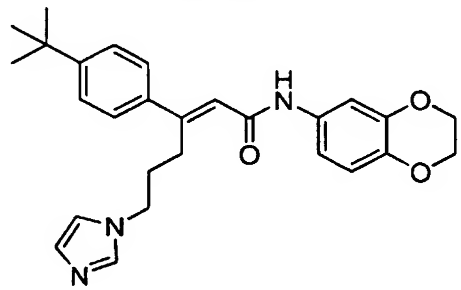


(b) Methyl (2Z)-3-[4-(tert-butyl)phenyl]-4-pyrrolidinylbut-2-enoate. A solution of methyl (2E)-3-[4-(*tert*-butyl)phenyl]but-2-enoate, **Example 91(a),** (0.37 g, 1.6 mmol) in CCl_4 (15 mL), magnetically stirred in a 50 mL round-bottomed flask under N_2, was treated with *N*-bromosuccinimide (0.31 g, 1.75 mmol, Aldrich) and 2,2'-azobisisobutyronitrile (5 mg, 0.03 mmol, Aldrich). The reaction mixture was magnetically stirred under reflux overnight, then allowed to cool to 25 °C. The solid was filtered. The filtrate was concentrated in vacuo to afford a yellow oil [MS (ESI, pos. ion) *m/z*: 311, 313 (M+1, M+3)]. To a solution of the yellow oil in THF (5 mL), was added pyrrolidine (0.16 mL, 1.9 mmol, Aldrich) and *N,N*-diisopropylethylamine (0.33 mL, 1.9 mmol, Aldrich). The reaction mixture was magnetically stirred at room temperature overnight, then concentrated in vacuo. The residue was treated with water and extracted with dichloromethane (3 x). The organic phase was dried over Na_2SO_4, filtered and concentrated in vacuo to afford a yellow oil. Purification by silica gel chromatography (gradient: 4%-20% EtOAc/hexane) provided the title product as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 302 (M+1).

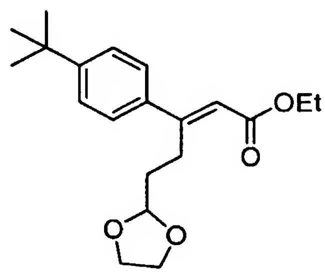
(c). N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-4-pyrrolidinylbut-2-enamide. To a 50 mL round-bottomed flask charged with methyl (2Z)-3-[4-(*tert*-butyl)phenyl]-4-pyrrolidinylbut-2-enoate, **Example 91(b),** (188 mg, 0.62 mmol) was added THF (2 mL), MeOH (0.2 mL), H_2O (1 mL), and lithium hydroxide monohydrate (54 mg, 1.25 mmol, Aldrich). The reaction mixture was magnetically stirred at room temperature overnight. The excess lithium hydroxide was removed by filtration. The mixture was purified by reverse phase preparative HPLC (CH_3CN/H_2O with 0.1%TFA), concentrated in vacuo, then treated with an excess of HCl in Et_2O. Concentration in vacuo provided a pale yellow solid 0.15 g [MS (ESI, pos. ion) *m/z*: 288 (M+1)]. Analogous to the procedure used to prepare **Example 1,** the solid (77 mg) and 1,4-benzodioxan-6-amine (61 mg, 0.40 mmol, Aldrich) provided the crude title product. Purification by silica gel chromatography (gradient: 1-5% MeOH in CH_2Cl_2) was followed by reverse phase preparative HPLC (CH_3CN/H_2O with 0.1%TFA). The fractions containing desired product were neutralized with $NaHCO_3$. The mixture was

extracted with CH_2Cl_2 and the organic phase concentrated in vacuo to provide the title product as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 421 (M+1).

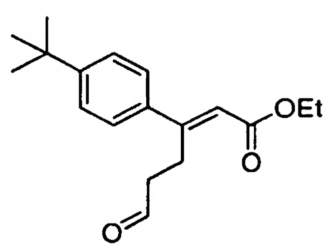
Example 92



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-6-imidazolylhex-2-enamide.

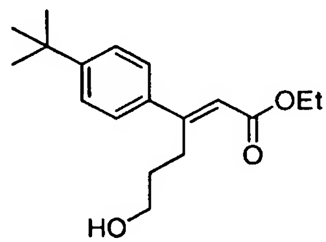


(a). Ethyl (2E)-3-[4-(tert-butyl)phenyl]-5-(1,3-dioxolan-2-yl)pent-2-enoate. Analogous to the procedure used to prepare **Example 53(a)**, starting from (1,3-dioxolan-2-ylethyl)zinc bromide (0.5 M THF solution, 40 mL, 20mmol, Rieke) and ethyl (2Z)-3-[4-(*tert*-butyl)phenyl]-3-iodoprop-2-enoate, **Example 52(b),** (3.58 g, 10.0 mmol), the title product was obtained as a colorless oil. MS (ESI, pos. ion) *m/z*: 333 (M+1).

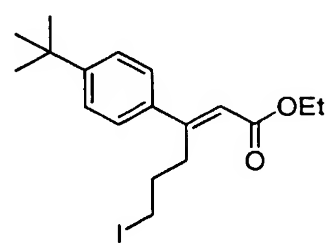


(b). Ethyl (2E)-3-[4-(tert-butyl)phenyl]-6-oxohex-2-enoate. To a round-bottomed flask was added ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-5-(1,3-dioxolan-2-yl)pent-2-enoate, **Example 92(a)**, (2.7 g, 8.1 mmol), THF (3 mL), and 5 N HCl (12 mL). The reaction mixture was initially stirred at room temperature for 24 h,

then heated to 40 °C overnight. The pH was adjusted to ~5-6 by the addition of $NaHCO_3$ and the mixture was extracted with EtOAc. The combined organic extract was dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel chromatography (5% EtOAc/hexane) provided the title product as a white solid. MS (ESI, pos. ion) *m/z*: 289 (M+1).

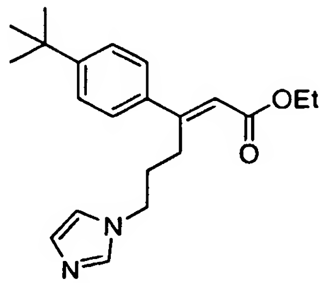


(c). Ethyl (2E)-3-[4-(tert-butyl)phenyl]-6-hydroxyhex-2-enoate. To solution of ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-6-oxohex-2-enoate, **Example 92(b),** (1.5 g, 5.3 mmol) in MeOH (18 mL), magnetically stirred at 0 °C in a 100 mL round-bottomed flask, was added sodium borohydride (0.40 g, 11 mmol, Aldrich). The mixture was allowed to gradually warm up to room temperature over 2 h, then quenched with water (20 mL) and extracted with EtOAc (4 x). The organic extract was dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel chromatography (15% EtOAc/hexane) provided the title product as a colorless oil in quantitative yield. MS (ESI, pos. ion) *m/z*: 291 (M+1).

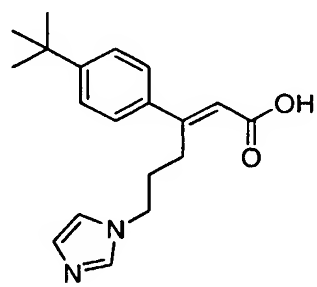


(d). Ethyl (2E)-3-[4-(tert-butyl)phenyl]-6-iodohex-2-enoate. To a 100 mL round-bottomed flask charged with ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-6-hydroxyhex-2-enoate, **Example 92(c)**, (0.80 g, 2.7 mmol) and CH_2Cl_2 (10 mL) at room temperature, was added triphenylphosphine (0.87 g, 3.3 mmol, Aldrich), imidazole (0.22 g, 3.3 mmol, Aldrich), and I_2 (1.2 g, 4.7 mmol, Aldrich). The reaction mixture was stirred for 2 h, filtered and concentrated in vacuo. Purification by silica gel chromatography (3% EtOAc/hexane) provided the title

product as a white semi-solid in quantitative yield. MS (ESI, pos. ion) *m/z*: 401 (M+1).



(e) Ethyl (2E)-3-[4-(tert-butyl)phenyl]-6-imidazolylhex-2-enoate. To a 100 mL round-bottomed flask charged with ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-6-iodohex-2-enoate, **Example 92(d),** (1.1 g, 2.7 mmol), imidazole (0.20 g, 3.0 mmol, Aldrich), benzyltriethylammonium chloride (63 mg, 0.30 mmol, Aldrich), and CH_2Cl_2 (15 mL), stirred magnetically at room temperature, was added potassium hydroxide (50% aqueous solution, 1.5 mL). The reaction mixture was stirred at 50 °C overnight, then diluted with water. The reaction mixture was extracted with CH_2Cl_2. The organic solution was dried over Na_2SO_4, filtered, and concentrated in vacuo. Purification by silica gel chromatography (50% EtOAc/hexane) provided the title product as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 341 (M+1).

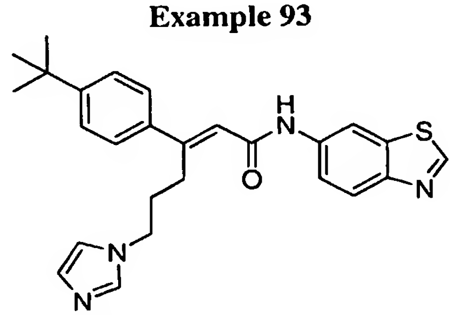


(f) (2E)-3-[4-(tert-Butyl)phenyl]-6-imidazolylhex-2-enoic acid. To a 50 mL round-bottomed flask equipped with a reflux condenser was added ethyl (2E)-3-[4-(*tert*-butyl)phenyl]-6-imidazolylhex-2-enoate, **Example 92(e)**, (0.35 g, 1.0 mmol), THF (6 mL) and KOH (50% aqueous solution, 1.5 mL). The reaction mixture was heated and magnetically stirred under reflux overnight, then concentrated in vacuo and acidified with glacial acetic acid to pH ~4-5. The aqueous mixture was extracted with CH_2Cl_2 and the organic phase was dried over

Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (5%-10% MeOH/CH_2Cl_2) provided the title product as a white solid. MS (ESI, pos. ion) *m/z*: 313 (M+1).

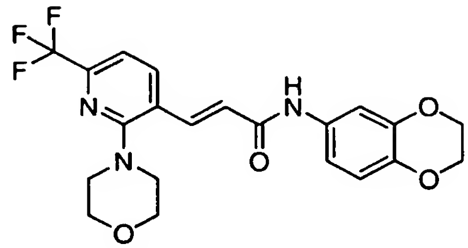
(g) (2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-6-imidazolylhex-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[4-(*tert*-butyl)phenyl]-6-imidazolylhex-2-enoic acid, **Example 92(f),** (76 mg, 0.24 mmol) and 1,4-benzodioxan-6-amine (36 mg, 0.24 mmol, Aldrich) provided, after purification by silica gel chromatography (3% -5% MeOH/CH_2Cl_2), the title product as an amorphous off-white solid. MS (ESI, pos. ion) *m/z*: 446 (M+1).

Example 93

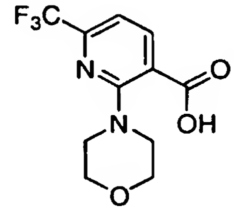


3-(4-tert-Butyl-phenyl)-6-imidazol-1-yl-hex-2-enoic acid benzothiazol-6-ylamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[4-(*tert*-butyl)phenyl]-6-imidazolylhex-2-enoic acid, **Example 92(f),** (76 mg, 0.24 mmol) and 6-aminobenzothiazole (36 mg, 0.24 mmol, Lancaster) provided, after purification by silica gel chromatography (3% -5% MeOH/CH_2Cl_2), the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 445 (M+1).

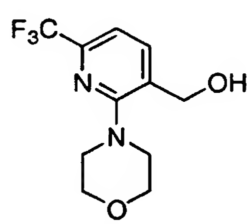
Example 94



(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[2-morpholin-4-yl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide.

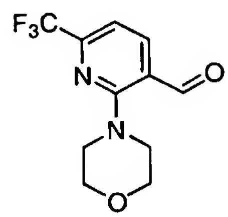


(a) 2-Morpholin-4-yl-6-(trifluoromethyl)pyridine-3-carboxylic acid. To a round-bottomed flask was added 2-chloro-6-trifluoromethylnicotinic acid (2.0 g, 8.9 mmol, Matrix) and morpholine (5.0 g, 57 mmol, Aldrich). The reaction mixture was magnetically stirred at 25 °C for 48 h, then diluted with 1 N HCl (100 mL) and extracted with EtOAc (100 mL). The aqueous phase was saturated with NaCl and extracted again with EtOAc (50 mL). The combined EtOAc extracts were washed with 1 N HCl (50 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to afford the title product as an off-white waxy solid. MS (ESI, pos. ion) m/z: 277 (M+1).

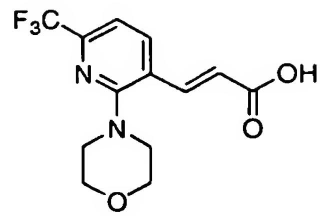


(b) [2-Morpholin-4-yl-6-(trifluoromethyl)-3-pyridyl]methan-1-ol. A solution of 2-morpholin-4-yl-6-(trifluoromethyl)pyridine-3-carboxylic acid, **Example 94(a)**, (2.1 g, 7.6 mmol) in anhydrous THF (20 mL) was treated dropwise with lithium aluminum hydride (15 mL, 15 mmol, 1.0 M in THF, Aldrich) with stirring under N_2 at 25 °C. The reaction mixture was stirred at 25 °C for 1.5 h, then quenched by the dropwise addition of a 10% aqueous solution of Rochelle salt

(50 mL, potassium sodium tartrate, Aldrich). EtOAc (50 mL) was added and the bi-phasic mixture stirred vigorously for 2 h at 25 °C. The mixture was diluted with water (100 mL) and the phases separated. The aqueous phase was extracted with EtOAc (2 x 75 mL), the organic phases were combined and washed with 1 N NaOH (2 x 75 mL), satd NaCl (75 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to afford the title product as a viscous yellow oil. MS (ESI, pos. ion) m/z: 263 (M+1).



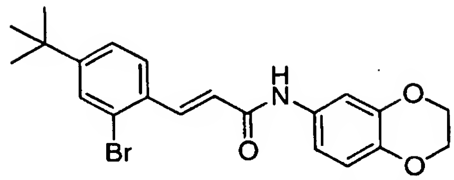
(c) 2-Morpholin-4-yl-6-(trifluoromethyl)pyridine-3-carbaldehyde. A solution of oxalyl chloride (3.6 mL, 7.2 mmol, 2.0 M in CH_2Cl_2, Aldrich) in anhydrous CH_2Cl_2 (20 mL) was magnetically stirred under N_2, in an oven-dried round-bottomed flask, at –60 °C. The solution was treated dropwise with methyl sulfoxide (1.1 mL, 15 mmol, Aldrich) then stirred for 10 min. A solution of [2-morpholin-4-yl-6-(trifluoromethyl)-3-pyridyl]methan-1-ol, **Example 94(b)**, (1.7 g, 6.5 mmol) in anhydrous CH_2Cl_2 (20 mL) was added via cannula, and the reaction mixture stirred at –60 °C for 15 min. Triethylamine (4.5 mL, 32 mmol, Aldrich) was added, the cooling bath was removed, and the reaction mixture allowed to warm to 25 °C and stirred at that temperature for 1 h. The mixture was washed with water (30 mL) and the aqueous wash was back-extracted with CH_2Cl_2 (2 x 20 mL). The combined organic phase was washed with water (30 mL), satd NaCl (30 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (9:1 hexane:EtOAc) provided the title product as a viscous yellow oil. MS (ESI, pos. ion) m/z: 261 (M+1).



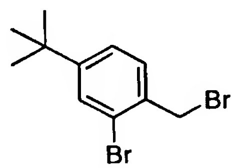
(d) (2E)-3-[2-Morpholin-4-yl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid. Analogous to the procedure described for **Example 40**, step (a), 2-morpholin-4-yl-6-(trifluoromethyl)pyridine-3-carbaldehyde, **Example 94(c),** (1.2 g, 4.6 mmol) provided the title product as a yellow solid. MS (ESI, pos. ion) m/z: 303 (M+1).

(e) (2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[2-morpholin-4-yl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide. (2E)-3-[2-Morpholin-4-yl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enoic acid, **Example 94(d),** (200 mg, 0.66 mmol) was dissolved in anhydrous CH_2Cl_2 (10 mL) and treated with oxalyl chloride (0.36 mL, 0.72 mmol, 2.0 M in CH_2Cl_2, Aldrich) and anhydrous DMF (2 uL). The reaction mixture was stirred at reflux for 30 min, then concentrated in vacuo. The residue was dissolved in anhydrous CH_2Cl_2 (10 mL), treated with pyridine (0.27 mL, 3.5 mmol, Aldrich) and 1,4-benzodioxan-6-amine (120 mg, 0.79 mmol, Aldrich) and stirred at reflux for 15 min. The reaction mixture was concentrated in vacuo and the residue dissolved in EtOAc (75 mL). The mixture was washed with 1 N HCl (2 x 50 mL), 1 N NaOH (50 mL), water (50 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Recrystallization from EtOAc and hexane provided the title product as pale tan crystals. MP 200-201 °C. MS (ESI, pos. ion) m/z: 436 (M+1).

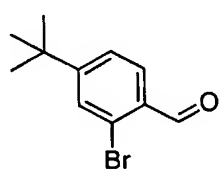
Example 95



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)-2-bromophenyl]prop-2-enamide.

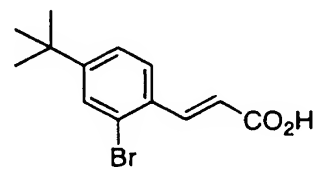


(a) 4-(tert-Butyl)-2-bromo-1-(bromomethyl)benzene. According to the procedure of Kikuchi, D. et al, *J. Org. Chem.* **1998**, *63*, 6023-6026, to a solution of sodium bromate (22 g, 145 mmol, Aldrich) in water (75 mL), magnetically stirred in an Erlenmeyer flask at 25 °C, was added a solution of 4-*t*-butyltoluene (5.0 mL, 29 mmol, Aldrich) in acetonitrile (60 mL). The bi-phasic mixture was vigorously stirred while a solution of sodium bisulfite (15 g, 145 mmol, Baker) in water (150 mL) was added dropwise, via addition funnel, over 20 min. The reaction mixture was stirred for 6 h, then extracted with Et_2O (300 mL). The organic phase was washed with satd aq. $Na_2S_2O_3$ (2 x 100 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to afford of the title product as a pale orange oil.



(b) 4-(tert-Butyl)-2-bromobenzaldehyde. According to the procedure of Mallory, et al, *Tetrahedron* **2001**, *57*, 3715-3724, a solution of sodium ethoxide (12 mL, 32 mmol, 21% in EtOH, Aldrich) in absolute EtOH (100 mL) was magnetically stirred under N_2 at 25 °C and treated with 2-nitropropane (2.9 mL, 32 mmol, Aldrich) followed by 4-(*tert*-butyl)-2-bromo-1-(bromomethyl)benzene, **Example 95(a)**, (9.0 g, 29 mmol). The reaction mixture was stirred at 25 °C for 5 h, then concentrated in vacuo to an orange solid. The solid was partitioned

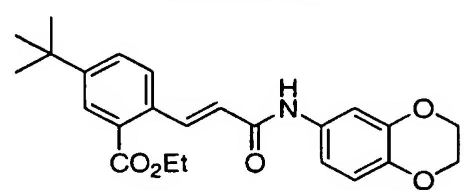
between Et_2O (150 mL) and water (100 mL). The layers were separated and the organic phase was washed with water (100 mL), 1 N NaOH (2 x 75 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated in vacuo to afford the title product as an orange oil.



(c) (2E)-3-[4-(tert-Butyl)-2-bromophenyl]prop-2-enoic acid. Analogous to the procedure described for **Example 40**, step (a), 4-(*tert*-butyl)-2-bromobenzaldehyde, **Example 95(b),** (6.5 g, 27 mmol) provided the title product as a white solid. MS (ESI, pos. ion) m/z: 283, 285 (M, M+2).

(d) (2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)-2-bromophenyl]prop-2-enamide. Analogous to the procedure described for **Example 94**, step (e), (2E)-3-[4-(*tert*-butyl)-2-bromophenyl]prop-2-enoic acid, **Example 95(c),** (3.0 g, 11 mmol) and 1,4-benzodioxan-6-amine (1.9 g, 13 mmol, Aldrich) provided, after recrystallization from CH_2Cl_2 and hexane, the title product as off-white crystals. MP 206-210 °C. MS (ESI, pos. ion) m/z: 416, 418 (M, M+2).

Example 96

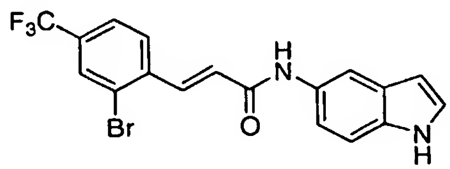


Ethyl 2-[(1E)-2-(N-(2H,3H-benzo[e]1,4-dioxan-6-yl)carbamoyl)vinyl]-5-(tert-butyl)benzoate.

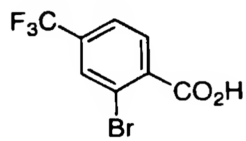
According to the procedure of Ma, et al, *J. Org. Chem.* **1999**, *64*, 120-125, a solution of (2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(*tert*-butyl)-2-bromophenyl]prop-2-enamide, **Example 95**, (200 mg, 0.48 mmol) in anhydrous EtOH (5 mL) and methyl sulfoxide (5 mL) was treated with triethylamine (0.67 mL, 0.48 mmol, Aldrich) and 1,3-bis(diphenylphosphino)propane (50 mg, 0.12 mmol, Aldrich). The mixture was purged with a stream of carbon monoxide, then treated with palladium acetate (22 mg, 0.10 mmol, Aldrich), and stirred

under a balloon of carbon monoxide in a 70 °C oil bath for 3 h. The reaction mixture was allowed to cool to 25 °C and partitioned between EtOAc (50 mL) and water (20 mL). The organic phase was washed with water (10 mL), satd NaCl (10 mL), dried over $MgSO_4$, filtered and concentrated in vacuo. Purification by silica gel chromatography (step gradient, 4:1 then 3:1, hexane:EtOAc), followed by recrystallization from EtOAc and hexane, provided the title product as white crystals. MP 155 °C. MS (ESI, pos. ion) m/z: 410 (M+1).

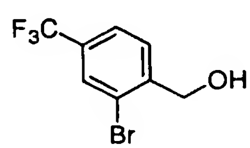
Example 97



(2E)-3-[2-Bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide.

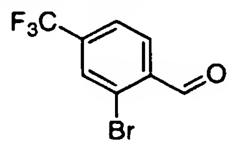


(a) 2-Bromo-4-(trifluoromethyl)benzoic acid. To a solution of 2-bromo-1-methyl-4-trifluoromethylbenzene (7.6 g, 32 mmol, ABCR) in pyridine (75 mL) was added tetraethylammonium permanganate (24 g, 96 mmol, prepared according to the procedure of Sala, et al. *J. Chem. Soc., Chem. Comm.* **1978**, 253). The reaction mixture was warmed to 70 °C and stirred at that temperature for 30 h. The reaction mixture was allowed to cool to 25 °C and poured into an ice bath containing cond HCl (150 mL) and $NaHSO_3$ (150 g). The mixture turned to a clear aqueous solution and was extracted with EtOAc (4 x 200 mL). The combined extracts were washed with satd NaCl (200 mL), dried over Na_2SO_4, filtered and concentrated in vacuo to provide the title product as a white solid. MS (ESI, neg. ion) *m/z*: 267 (M-1).

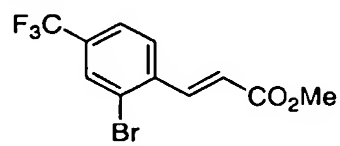


(b) [2-Bromo-4-(trifluoromethyl)phenyl]methan-1-ol. Analogous to the procedure used to prepare **Example 46**, step (a), 2-bromo-4-

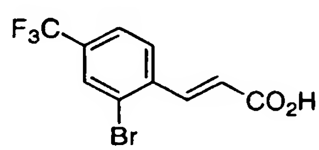
(trifluoromethyl)benzoic acid, **Example 97(a),** (5.4 g, 20 mmol) provided, after purificaton by silica gel chromatography (gradient: 0-10% EtOAc in hexane), the title product as a white solid. MS (ESI, neg. ion) *m/z*: 313 (M+acetate).



(c) 2-Bromo-4-(trifluoromethyl)benzaldehyde. Analogous to the procedure used to prepare **Example 46**, step (b), [2-bromo-4-(trifluoromethyl)phenyl]methan-1-ol, **Example 97(b),** (4.6 g, 18 mmol) provided, after purificaton by silica gel chromatography (gradient: 0-4% EtOAc in hexane), the title product as a colorless oil.



(d) Methyl (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoate. Analogous to the procedure used to prepare **Example 46**, step (c), 2-bromo-4-(trifluoromethyl)benzaldehyde, **Example 97(c),** (2.3 g, 8.9 mmol) and carbomethoxymethylene triphenylphosphorane (4.2 g, 12.5 mmol, Aldrich) provided, after purificaton by silica gel chromatography (gradient: 0-3% EtOAc in hexane), the title product as a white solid.

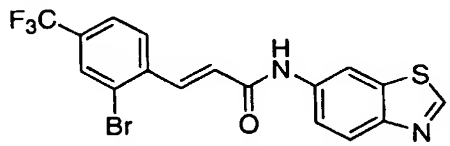


(e) (2E)-3-[2-Bromo-4-(trifluoromethyl)phenyl]prop-2-enoic acid. Analogous to the procedure used to prepare **Example 46**, step (d), methyl (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoate, **Example 97(d),** (2.25 g, 8.9 mmol) provided the title product.

(f) (2E)-3-[2-Bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 97(e),** (140 mg, 0.48 mmol) and 5-aminoindole (75 mg, 0.57 mmol, Aldrich) provided, after purification by

silica gel chromatography (gradient: 0-25% EtOAc in hexane), the title compound as a yellow solid. MP 205-207 °C. MS (ESI, pos. ion) *m/z*: 409 (M+1).

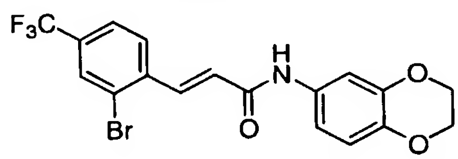
Example 98



(2E)-N-Benzothiazol-6-yl-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 97(e)**, (140 mg, 0.47 mmol) and 6-aminobenzothiazole (86 mg, 0.57 mmol, Lancaster) provided, after purification by silica gel chromatography (gradient: 0-30 % EtOAc in hexane), the title product as an off-white solid. MP 214-215 °C. MS (ESI, pos. ion) *m/z*: 427 (M+1).

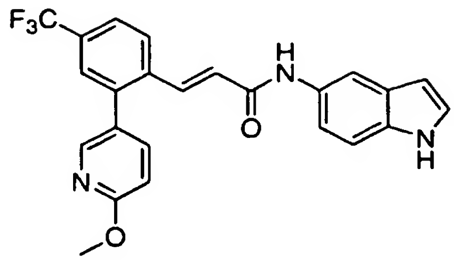
Example 99



(2E)-N-(2H,3H-Benzo[e]1,4-dioxan-6-yl)-3-[2-bromo-4-(trifluoromethyl)-phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 97(e)**, (140 mg, 0.47 mmol) and 1,4-benzodioxan-6-amine (86 mg, 0.57 mmol, Aldrich) provided, after purification by silica gel chromatography (gradient: 0-18 %EtOAc in hexane), the title product as an off-white solid. MP 212-213 °C. MS (ESI, pos. ion) *m/z*: 428 (M+1).

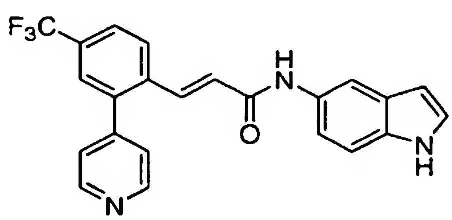
Example 100



(2E)-N-indol-5-yl-3-[2-(6-methoxy(3-pyridyl))-4-(trifluoromethyl)phenyl]-prop-2-enamide.

A mixture of (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (100 mg, 0.24 mmol), 2-methoxy-5-pyridineboronic acid (60 mg , 0.39 mmol, Digital Specialty Chemicals), tris(dibenzylideneacetone)-dipalladium(0) (22 mg, 0.024 mmol, Aldrich) and triphenylphosphine (26 mg, 0.098 mmol, Aldrich) in toluene (1.2 mL), 2.0M aqueous Na_2CO_3 (0.4 mL) and ethanol (0.4 mL) was stirred at 120 °C overnight. The reaction mixture was filtered through a pad of Celite and diluted with water (50 mL). The aqueous phase was extracted with EtOAc (3 x 60 mL). The combined extracts were washed with satd NaCl (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (gradient: 0-20% EtOAc in hexane) provided the title product as a yellow solid. MP 219-221 °C. MS (ESI, pos. ion) *m/z*: 438 (M+1).

Example 101

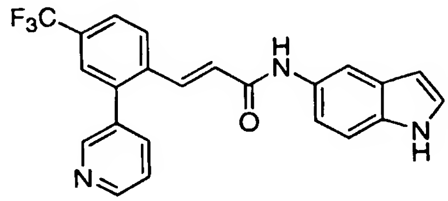


(2E)-N-Indol-5-yl-3-[2-(4-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 100**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (120 mg, 0.29 mmol) and pyridine-4-boronic acid (72 mg, 0.59 mmol, Frontier Scientific) provided, after purification by silica gel chromatography (gradient: 0-60 %EtOAc

in hexane), the title product as a yellow solid. MP 229-234 °C. MS (ESI, pos. ion) *m/z*: 408 (M+1).

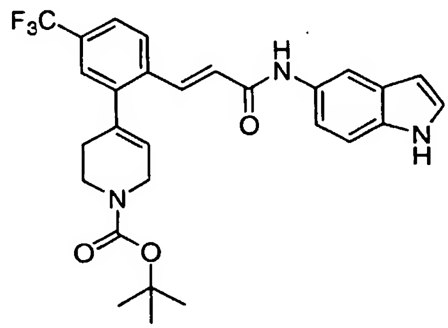
Example 102



(2E)-N-Indol-5-yl-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 100**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (120 mg, 0.29 mmol) and pyridine-3-boronic acid (58 mg, 0.47 mmol, Frontier Scientific) provided, after purification by silica gel chromatography (gradient: 0-20 %EtOAc in hexane), the title product as a yellow solid. MP 196-197 °C. MS (ESI, pos. ion) *m/z*: 408 (M+1).

Example 103

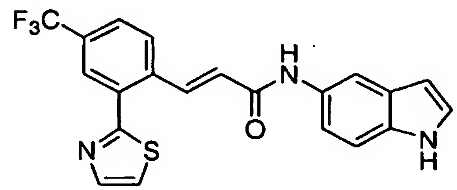


tert-Butyl 4-{2-[(1E)-2-(N-indol-5-ylcarbamoyl)vinyl]-5-(trifluoromethyl)phenyl}-1,2,5,6-tetrahydropyridinecarboxylate.

Analogous to the procedure used to prepare **Example 100**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (100 mg, 0.24 mmol) and 4-(4,4,5,5-tetramethyl-[1,3,2]dioxaborolan-2-yl)-3,6-dihydro-2H-pyridine-1-carboxylic acid *tert*-butyl ester (130 mg, 0.42 mmol, prepared according to the procedures of Wustrow, D. J. et al, *Synthesis* 1991, 993 and Ishiyama, T. et al, *J. Org. Chem.* 1995, *60*, 7508) provided, after purification by

silica gel chromatography (gradient: 0-35 %EtOAc in hexane), the title product as an amorphous yellow solid. MS (ESI, pos. ion) *m/z*: 512 (M+1).

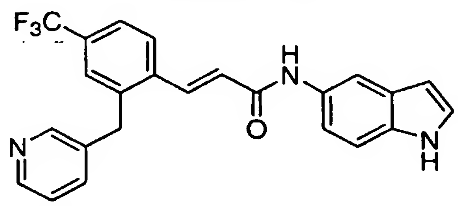
Example 104



(2E)-N-Indol-5-yl-3-[2-(1,3-thiazol-2-yl)-4-(trifluoromethyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 100**, (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (100 mg, 0.24 mmol) and 2-tributylstannylthiazole (155 mg, 0.42 mmol, Frontier Scientific) provided, after purification by silica gel chromatography (gradient: 0-35 %EtOAc in hexane), the title product as an orange solid. MP 203-204 °C. MS (ESI, pos. ion) *m/z*: 414 (M+1).

Example 105

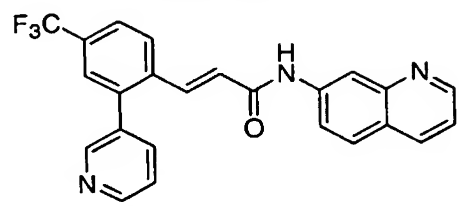


(2E)-N-Indol-5-yl-3-[2-(3-pyridylmethyl)-4-(trifluoromethyl)phenyl]prop-2-enamide.

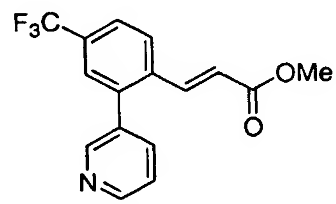
A mixture of (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide, **Example 97**, (110 mg, 0.27 mmol), 3-(tributylstannanylmethyl)pyridine, **Example 90(a)**, (160 mg, 0.43 mmol), tris(dibenzylideneacetone)dipalladium(0) (24 mg, 0.027 mmol, Aldrich) and triphenylphosphine (28 mg, 0.11 mmol, Aldrich) in 1-methyl-2-pyrrolidinone (1.5 mL) was stirred at 100 °C overnight. The reaction mixture was filtered through a pad of Celite and diluted with water (50 mL). The aqueous phase was extracted with EtOAc (3 x 60 mL). The combined organic extracts were washed with satd NaCl (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (gradient: 0-70 % EtOAc in hexane)

provided the title compound as an orange solid. MP 202-203 °C. MS (ESI, neg. ion) *m/z*: 420 (M-1).

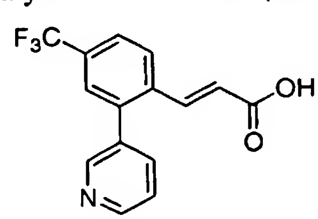
Example 106



(2E)-3-[2-(3-Pyridyl)-4-(trifluoromethyl)phenyl]-N-(7-quinolyl)prop-2-enamide.



(a) Methyl (2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoate. A mixture of methyl (2E)-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enoate, **Example 97(d),** (585 mg, 1.89 mmol), pyridine-3-boronic acid (950 mg, 2.8 mmol, Frontier Scientific), tris(dibenzylideneacetone)dipalladium (0) (170 mg, 0.19 mmol, Aldrich) and triphenylphosphine (200 mg, 0.76 mmol, Aldrich) in toluene (5 mL), 1.0 M aqueous Na_2CO_3 (2 mL) and ethanol (2 mL) was stirred at 80 °C under N_2 overnight. The reaction mixture was filtered through a pad of Celite and diluted with water (60 mL). The aqueous phase was extracted with EtOAc (3 x 60 mL). The combined organic extracts were washed with satd NaCl (100 mL), dried over Na_2SO_4, filtered and concentrated in vacuo. Purification by silica gel chromatography (gradient: 0-35% EtOAc in hexane) provided the title product as a yellow solid. MS (ESI, pos. ion) *m/z*: 308 (M+1).

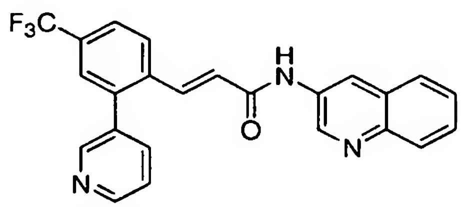


(b) (2E)-3-[2-(3-Pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoic acid. A mixture of methyl (2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoate,

Example 106(a), (540 mg, 1.8 mmol) and LiOH monohydrate (370 mg, 8.8 mmol) in wet ethanol (5 mL) was stirred at room temperature overnight. The reaction mixture was neutralized with aqueous HCl (2.0 M, 4.4 mL, 8.8 mmol) and concentrated under reduced pressure. The material was dried under vacuum at 60 °C for 4 h to provide 955 mg of the crude material, which contained LiCl as a byproduct. MS (ESI, pos. ion) *m/z*: 294 (M+1).

(c) (2E)-3-[2-(3-Pyridyl)-4-(trifluoromethyl)phenyl]-N-(7-quinolyl)prop-2-enamide. Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 106(b),** (185 mg) and 7-aminoquinoline (64 mg, 0.44 mmol, Specs) provided, after purification by silica gel chromatography (gradient: 0-75% EtOAc in hexane), the title compound as an amorphous off-white solid. MS (ESI, pos. ion) *m/z*: 420 (M+1).

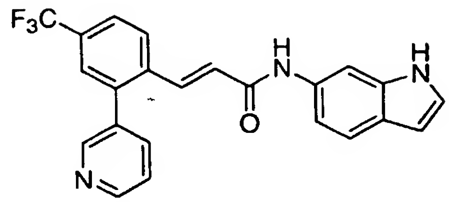
Example 107



(2E)-3-[2-(3-Pyridyl)-4-(trifluoromethyl)phenyl]-N-(3-quinolyl)prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 106(b),** (185 mg) and 3-aminoquinoline (64 mg, 0.44 mmol, Aldrich) provided, after purification by silica gel chromatography (gradient: 0-45% EtOAc in hexane), the title compound as a white solid. MP 196-199 °C. MS (ESI, pos. ion) *m/z*: 420 (M+1).

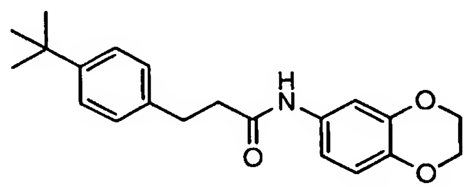
Example 108



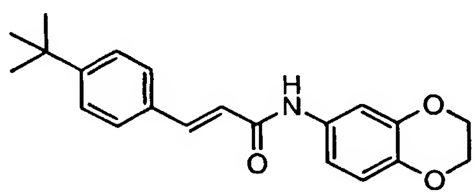
(2E)-N-Indol-6-yl-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide.

Analogous to the procedure used to prepare **Example 1**, (2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enoic acid, **Example 106(b),** (185 mg) and 6-aminoindole (59 mg, 0.44 mmol, Aldrich) provided, after purification by silica gel chromatography (gradient: 0-50% EtOAc in hexane), the title compound as an amorphous orange solid. MS (ESI, pos. ion) *m/z*: 408 (M+1).

Example 109



N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]propanamide.

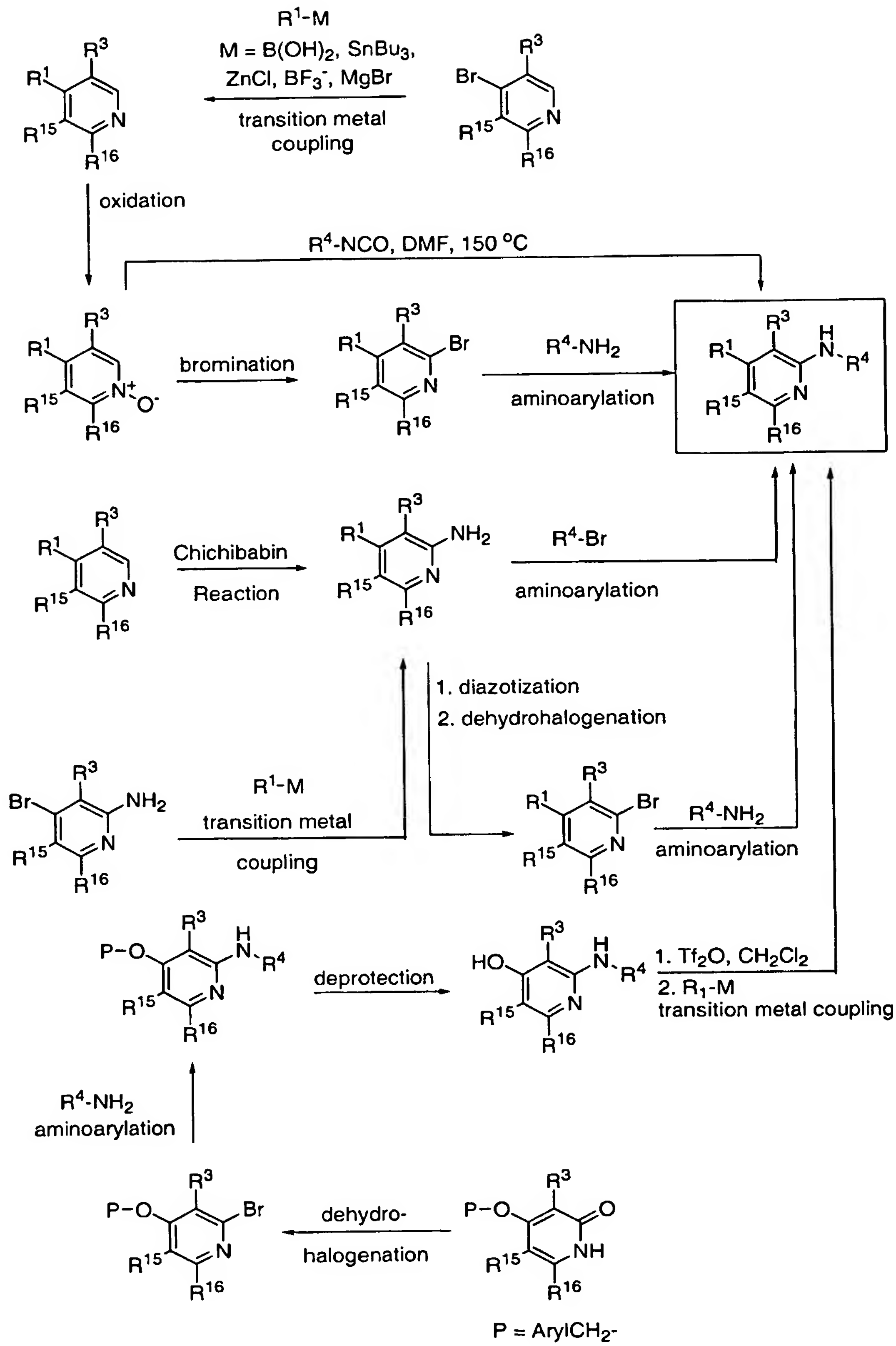


(a) (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-prop-2-enamide. A solution of 4-*t*-butyl-*trans*-cinnamic acid (500 mg, 2.45 mmol, EMKA-Chemie) in anhydrous CH_2Cl_2 (10 mL) was magnetically stirred and treated with oxalyl chloride (0.22 mL, 2.5 mmol, Aldrich) and DMF (0.005 mL). The reaction mixture was stirred at reflux for 30 min, then concentrated in vacuo. The residue was dissolved in acetone (1 mL) and added to a mixture of 1,4-benzodioxan-6-amine (370 mg, 2.45 mmol, Aldrich) and K_2CO_3 (500 mg) in acetone (2 mL) and water (4 mL), stirred at 0 °C. The reaction mixture was vigorously stirred at 0 °C for 30 min, then diluted with ice water (50 mL). The resulting solid precipitate was collected by filtration and dissolved

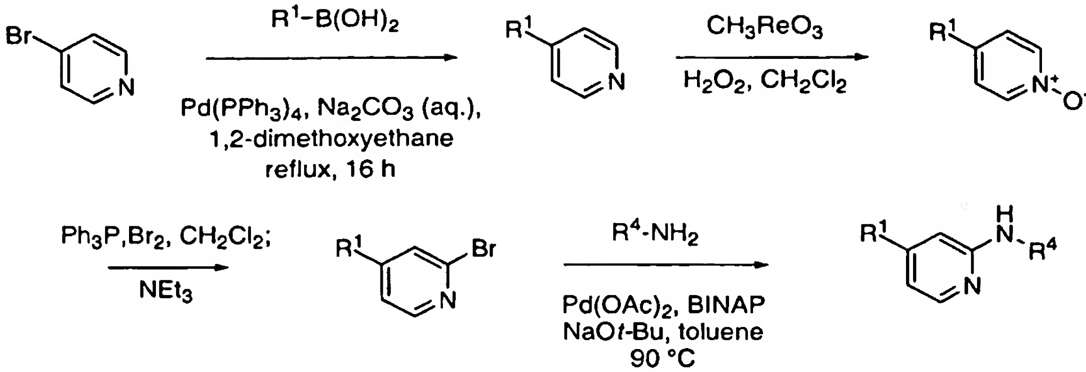
in CH_2Cl_2 (20 mL) and Et_2O (150 mL). The organic solution was washed with 1 N HCl (3 x 75 mL), satd NaCl (50 mL), dried over $MgSO_4$, filtered and concentrated to afford the title product as an off-white foam. MS (ESI, pos. ion) m/z: 338 (M+1).

(b) N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]propanamide. (2E)-N-(2H,3H-Benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide, **Example 109(a)**, (200 mg, 0.59 mmol) was dissolved in EtOH (25 mL), purged with N_2, treated with 10% Pd on carbon (50 mg, Aldrich) then purged with H_2 and the suspension stirred at 25 °C, under 1 atm H_2, for 16 hr. The suspension was purged with N_2, filtered through a pad of Celite, and concentrated *in vacuo* to a white foam. Purification by silica gel chromatography (45:45:10 hexane:CH_2Cl_2:EtOAc) provided the title product as a clear glass. MS (ESI, pos. ion) *m/z*: 340 (M+1).

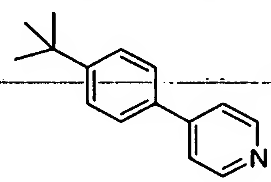
General Scheme I


R1-M
M = B(OH)2, SnBu3, ZnCl, BF3-, MgBr
transition metal coupling
oxidation
R4-NCO, DMF, 150 °C
bromination
R4-NH2
aminoarylation
Chichibabin Reaction
R4-Br
aminoarylation
1. diazotization
2. dehydrohalogenation
R1-M
transition metal coupling
R4-NH2
aminoarylation
deprotection
1. Tf2O, CH2Cl2
2. R1-M
transition metal coupling
R4-NH2
aminoarylation
dehydro-halogenation
P = ArylCH2-

General Scheme II

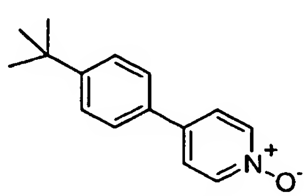


Example 110



(a) 4-[4-(*tert*-Butyl)phenyl]pyridine.

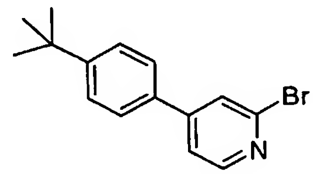
To 4-bromopyridine hydrochloride (Aldrich) (8.9 g, 46 mmol) and tetrakis(triphenylphosphine)palladium(0) (Aldrich) (1.6 g, 1.4 mmol) was added 1,2-dimethoxyethane (250 mL) with stirring under nitrogen. After 20 min, a solution of Na_2CO_3 (9.7 g in 70 mL of water) and 4-*tert*-butylbenzeneboronic acid (9.8 g, 55 mmol) were added sequentially to the mixture. The reaction was stirred at reflux overnight. The reaction mixture was concentrated in vacuo to approximately 1/3 its original volume, and the mixture was extracted with EtOAc (2 × 100 mL). The combined EtOAc layers were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by silica gel chromatography (1:5 EtOAc/hexanes) gave the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 212 (M+1).



(b) 4-[4-(*tert*-Butyl)phenyl]pyridine 1-oxide.

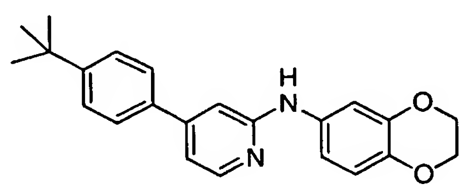
To the mixture of 4-[4-(*tert*-butyl)phenyl]pyridine (8.7 g, 41 mmol) and methyltrioxorhenium (VII) (Aldrich) (170 mg, 0.7 mmol) in a 100-mL round-

bottomed flask was added CH_2Cl_2 (18 mL). The mixture was then treated with 12 mL of hydrogen peroxide (Aldrich) dropwise. The reaction was stirred at room temperature under nitrogen overnight. Methylene chloride and brine were then added, and the aqueous layer was extracted with CH_2Cl_2 (40 mL). The organic layer was dried over Na_2SO_4, concentrated in vacuo to give the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 228 (M+1).



(c) 4-[4-(*tert*-Butyl)phenyl]-2-bromopyridine.

To triphenylphosphine (Aldrich) (2.4 g, 9.1 mmol) dissolved in 10 mL of CH_2Cl_2 in a 50-mL round-bottomed flask was added bromine (Aldrich) (0.43 mL, 8.5 mmol). After stirring at 0° C for 10 min, 4-[4-(*tert*-butyl)phenyl]pyridine 1-oxide (1.5 g, 6.5 mmol) was added dropwise, followed by Et_3N (1.2 mL, 8.5 mmol). The reaction mixture was stirred at 0° C for 1 h and then at room temperature overnight. Methylene chloride and brine were added, and the aqueous layer was extracted with CH_2Cl_2. The organic layer was collected and dried over Na_2SO_4, filtered and concentrated in vacuo. Following purification by silica gel chromatography (10:1 hexane:EtOAc), the title compound was obtained as a pale yellow oil. MS (ESI, pos. ion) *m/z*: 293 (M+1).

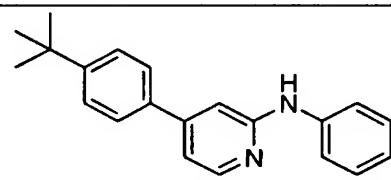
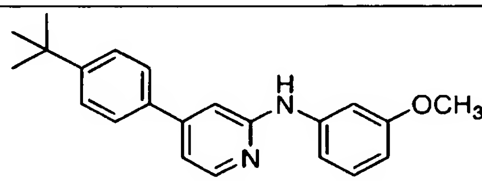
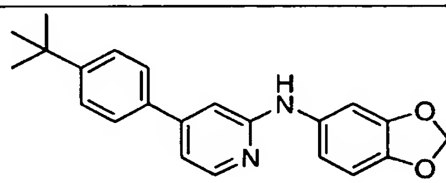
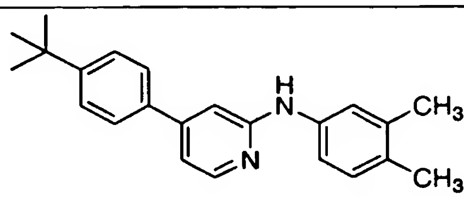


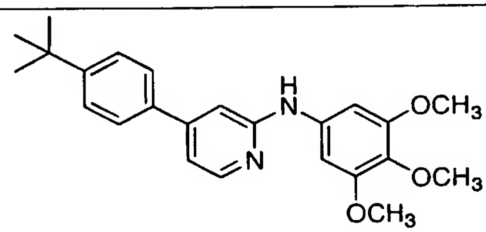
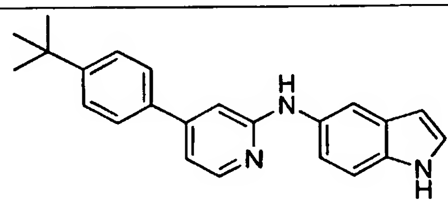
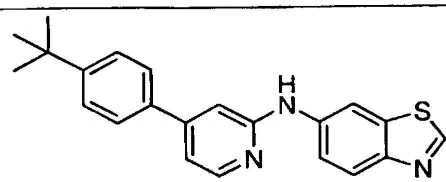
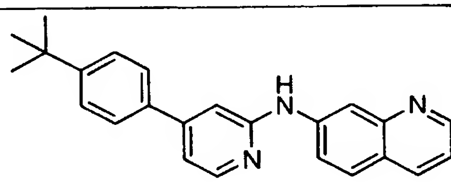
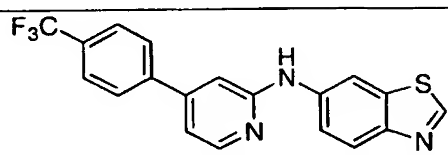
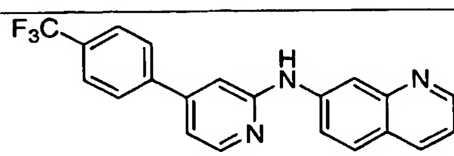
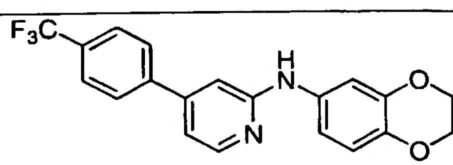
(d) 2H,3H-Benzo[e]1,4-dioxan-6-yl{4-[4-(*tert*-butyl)phenyl](2-pyridyl)}amine.

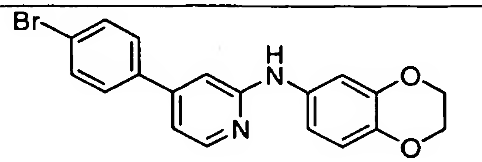
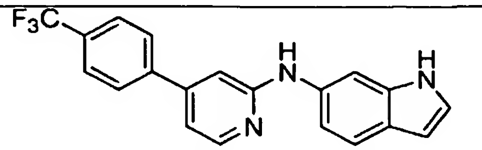
To an oven-dried 50-mL round-bottomed flask were added 4-[4-(*tert*-butyl)phenyl]-2-bromopyridine (180 mg, 0.63 mmol) and 1,4-benzodioxan-6-amine (Aldrich) (191 mg, 1.3 mmol), followed by anhydrous toluene (60 mL) and DMF (6 mL). Nitrogen was bubbled through the above solution via a needle for 1 h. Then palladium acetate (Aldrich) (21 mg, 0.01 mmol) and BINAP (Aldrich)

(59 mg, 0.01 mmol) were introduced to the reaction followed by sodium *tert*-butoxide (Aldrich) (170 mg, 1.8 mmol). The reaction mixture was heated in a 90 C oil bath overnight. After cooling to room temperature, the reaction mixture was dissolved in ether, washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Following purification by silica gel chromatography (3:1 hexane:EtOAc), the title compound was obtained as a pale tan solid. MS (ESI, pos. ion) *m/z*: 361 (M+1). MP: 162-163°C.

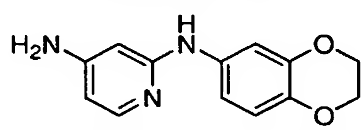
Table A. The following compounds were prepared according to General Schemes I and II:

Example	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
111		303 (M+1)	157
112		333 (M+1)	amorphous
113		347 (M+1)	156
114		331 (M+1)	133

Example	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
115		393 (M+1)	amorphous
116		342 (M+1)	106
117		360 (M+1)	154
118		354 (M+1)	214
119		372 (M+1)	203
120		366 (M+1)	206
121		373 (M+1)	114

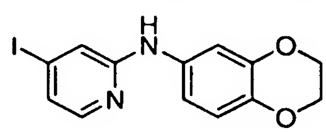
Example	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
122		383, 385 (M, M+2)	124
123		354 (M +1)	?

Example 124



(a) N2-(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-pyridine-2,4-diamine.

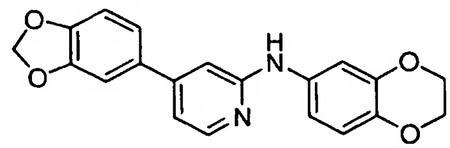
In a 5-mL vial was added 4-amino-2-chloropyridine (Aldrich Chemical Company) (1.1 g, 8.7 mmol), 1,4-benzodioxane-6-amine (Aldrich Chemical Company) (5.3 g, 35 mmol) and copper (I) iodide (Aldrich Chemical Company) (0.17 g, 0.87 mmol). The content was sonicated at room temperature for 5min and then heated in the Smith Microwave Synthesizer at 200 °C for 10 min. The residue was purified by flash chromatography (95:5 dichloromethane:2N NH_3 in MeOH) to give the title compound as a dark solid. MS (ESI, pos. ion) *m/z*: 244 (M+1).



(b) (2,3-Dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine.

Isopentyl nitrile (Aldrich Chemical Company) (3.9 mL, 29 mmol) was added to a mixture of N2-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-pyridine-2,4-diamine (Example 2(a), 2.4 g, 9.8 mmol), potassium iodide (Aldrich Chemical Company) (1.6 g, 9.8 mmol), iodine (Aldrich Chemical Company) (1.2 g, 4.9 mmol) and copper (I) iodide (Aldrich Chemical Company) (1.9 g, 9.8 mmol) in 1,2-dimethoxyethane (60 mL). The reaction mixture was heated at 60-65 °C for 1hr.

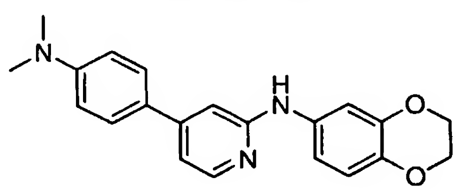
After cooling to room temperature, the insoluble materials were removed by filtration and the filtrate was diluted with EtOAc, washed with 25% aqueous NH_4OH, 5% aqueous sodium bisulfite and then brine. The organic layer was separated, dried over Na_2SO_4 and concentrated in vacuo. The residue was purified on a Biotage 40 M column (2.5:1 hexane:EtOAc) to give the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 355 (M+1).



(c) (4-Benzo[1,3]dioxol-5-yl-pyridin-2-yl)-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine.

In a 5 mL vial were added (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 2(b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol) and 1,2-dimethoxyethane (2 mL). After stirring under nitrogen for 10 min, aqueous Na_2CO_3 (22 mg in 0.5 mL of water) and 3,4-(methylenedioxy)phenylboronic acid (Aldrich Chemical Company) (42 mg, 0.25 mmol) were introduced. The reaction was heated in the Smith Microwave Synthesizer at 150 °C for 10 min. The residue was partitioned between EtOAc and brine. The aqueous layer was extracted with EtOAc and the combined EtOAc layer was washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification on a Biotage 40 S column (4:1 hexane:EtOAc) gave the title compound as a light-yellow solid. MS (ESI, pos. ion) *m/z*: 349 (M+1). Mp: 116.0-118.0 °C.

Example 125

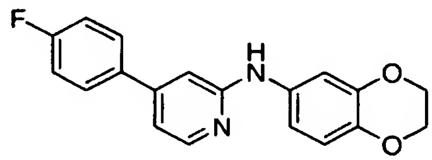


(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-dimethylamino-phenyl)-pyridin-2-yl]-amine.

Following the same procedure described for Example 401(c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401(b),

75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), N, N-dimethylaminobenzeneboronic acid (Aldrich Chemical Company) (41 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and purification on a Biotage 40S column (1.5:1 hexane:EtOAc), the title compound as a tan solid. MS (ESI, pos. ion) *m/z*: 348 (M+1). Mp: 154.0-155.5 °C.

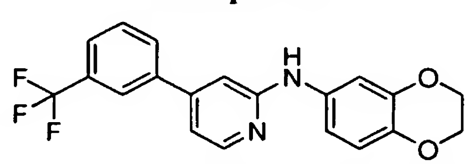
Example 126



(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-fluoro-phenyl)-pyridin-2-yl]-amine.

Following the same procedure described for Example 401 (c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401 (b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), 4-fluorobenzeneboronic acid (Avocado Chemical Company) (35 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and purification on a Biotage 40S column (3:1 hexane:EtOAc), the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 323 (M+1). Mp: 134.5-135.0 °C.

Example 127

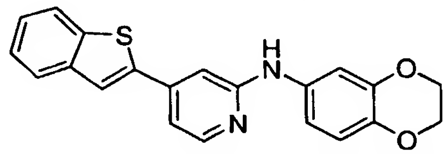


(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-[4-(3-trifluoromethyl-phenyl)-pyridin-2-yl]-amine.

Following the same procedure described for Example 401(c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401 (b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), 3-(trifluoromethyl)phenylboronic acid (Aldrich Chemical Company) (47 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and

purification on a Biotage 40S column (4:1 hexane:EtOAc), the title compound as a light-yellow solid. MS (ESI, pos. ion) *m/z*: 373 (M+1). Mp: 138.9-140.5 °C.

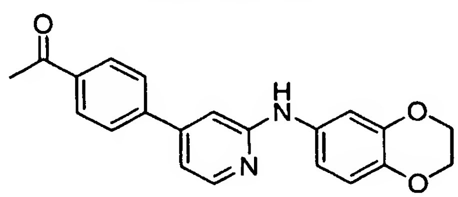
Example 128



(4-Benzo[b]thiophen-2-yl-pyridin-2-yl)-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine.

Following the same procedure described for Example 401(c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401(b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), benzothiophene-2-boronic acid (Frontier Scientific, Inc.) (45 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and purification on a Biotage 40S column (4:1 hexane:EtOAc), the title compound as a light-yellow solid. MS (ESI, pos. ion) *m/z*: 361 (M+1). Mp: 154.0-154.1 °C.

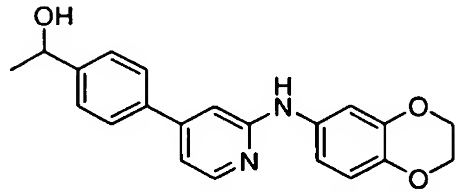
Example 129



1-{4-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-ylamino)-pyridin-4-yl]-phenyl}-ethanone.

Following the similar procedure described for Example 401(c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401 (b), 0.73 g, 2.1 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (0.12 g, 0.11 mmol), 4-actylphenylboronic acid (Aldrich Chemical Company) (0.41 g, 2.5 mmol) and 1,2-dimethoxyethane (20 mL) gave, after heated at 90 °C overnight and purification on a Biotage 40M column (3:1 hexane:EtOAc), the title compound as a light-orange solid. MS (ESI, pos. ion) *m/z*: 347 (M+1). Mp: 178.0-180.5 °C.

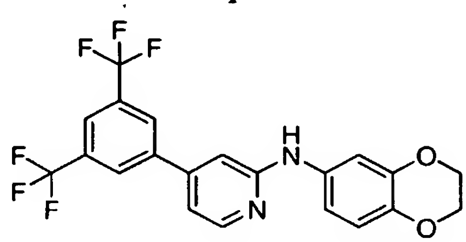
Example 130



1-{4-[2-(2,3-Dihydro-benzo[1,4]dioxin-6-ylamino)-pyridin-4-yl]-phenyl}-ethanol.

To the suspension of 1-{4-[2-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-pyridin-4-yl]-phenyl}-ethanone (Example 7, 0.19 g, 0.55 mmol) in 2 mL of MeOH was added a solution of methylamine in MeOH (Aldrich Chemical Company) (2N, 0.55mL, 1.1 mmol). The reaction was stirred at room temperature under nitrogen overnight. $NaBH_4$ (Aldrich Chemical Company) (25 mg, 0.66 mmol) was then added to the reaction and it was stirred for another 5 hrs. The solvent was evaporated the residue was purified on a Biotage 40M column (97:3 dichloromethane:2N NH_3 in MeOH) to give the title compound as an off-white foam. MS (ESI, pos. ion) *m/z*: 349 (M+1). Mp: 55.9- 61.5 °C.

Example 131

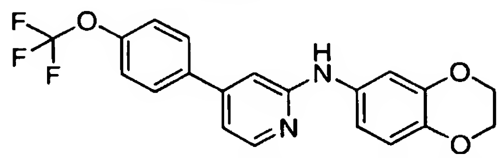


[4-(3,5-Bis-trifluoromethyl-phenyl)-pyridin-2-yl]-(2,3-dihydro-benzo[1,4]-dioxin-6-yl)-amine.

Following the same procedure described for Example 401 (c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401 (b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), 3,5-bis(trifluoromethyl)phenylboronic acid (Aldrich Chemical Company) (64 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and purification on a Biotage 40S column (4:1 hexane:EtOAc), the title

compound as a light-yellow solid. MS (ESI, pos. ion) *m/z*: 441 (M+1). Mp: 130.0-131.5 °C.

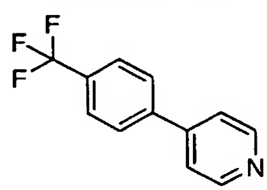
Example 132



(2,3-Dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-trifluoromethoxy-phenyl)-pyridin-2-yl]-amine.

Following the same procedure described for Example 401 (c), the mixture of (2,3-dihydro-benzo[1,4]dioxin-6-yl)-(4-iodo-pyridin-2-yl)-amine (Example 401 (b), 75 mg, 0.2 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich Chemical Company) (12 mg, 0.011 mmol), 4-(trifluoromethoxy)phenylboronic acid (Lancaster Synthesis Ltd.) (51 mg, 0.25 mmol) and 1,2-dimethoxyethane (2 mL) gave, after heated in the Microwave Smith Synthesizer at 150 °C for 10 min and purification on a Biotage 40S column (4:1 hexane:EtOAc), the title compound as an orange glass. MS (ESI, pos. ion) *m/z*: 389 (M+1).

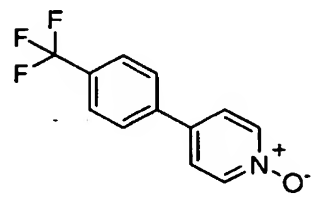
Example 133



(a) 4-(4-Trifluoromethyl-phenyl)-pyridine.

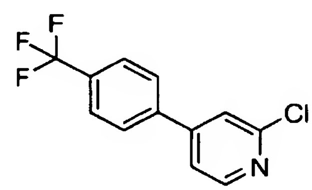
In a 250-mL, round-bottomed flask were added 4-bromopyridine hydrochloride (Aldrich) (4.7 g, 24 mmol), tetrakis (triphenylphosphine) palladium (0) (Aldrich) (1.4 g, 1.2 mmol) and 1,2-dimethoxyethane (120 mL). After stirring under nitrogen for 10 min, a solution of Na_2CO_3 (5.2 g in 30 mL of water) and 4-trifluoromethylbenzeneboronic acid (5.1 g, 27 mmol) were added sequentially to the mixture. The reaction was stirred in a 90 °C oil bath overnight. The 1,2-dimethoxyethane was evaporated in vacuo, and EtOAc was added to the residue. The aqueous layer was separated and extracted with EtOAc (2 x 50 mL). The combined EtOAc extracts were washed with brine, dried over Na_2SO_4 and concentrated in vacuo. Purification by silica gel flash chromatography using 1:5

EtOAc/hexanes as eluent gave the title compound as a light-tan solid. MS (ESI, pos. ion) *m/z*: 224 (M+1).



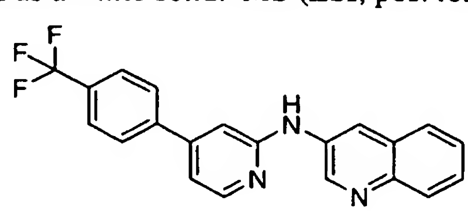
(b) 4-(4-Trifluoromethyl-phenyl)-pyridine 1-oxide.

To a mixture of 4-(4-trifluoromethyl-phenyl)-pyridine (5.0 g, 22 mmol) and methyltrioxorhenium (VII) (Aldrich) (110 mg, 0.45 mmol) in a 100-mL, round-bottomed flask was added CH_2Cl_2 (10 mL). Hydrogen peroxide (5 mL, Aldrich) was added drop-wise, and the reaction was stirred at room temperature under N_2 for 48 h. The mixture was partitioned between CH_2Cl_2 and brine, and the aqueous layer was extracted with CH_2Cl_2 (40 mL). The combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo to give the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 240 (M+1).



(c) 2-Chloro-4- (4-trifluoromethyl-phenyl)-pyridine.

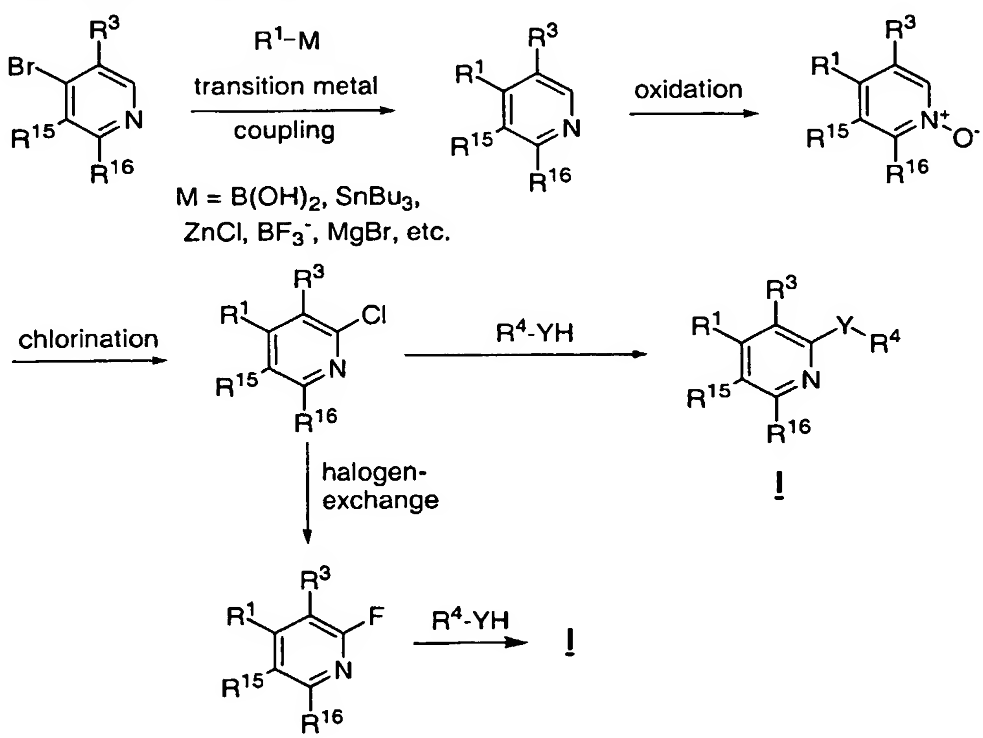
To 4-(4-trifluoromethyl-phenyl)-pyridine 1-oxide (2.4 g, 10 mmol) was added phosphorous oxychloride (12 mL) at room temperature. The reaction mixture was heated at reflux for 5 h. $POCl_3$ was removed under reduced pressure, and the residue was partitioned between EtOAc and aqueous ammonium hydroxide. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The crude material was purified by chromatography on a Biotage 40 M column (8:1 hexanes: EtOAc) to give the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 258.5 (M+1).



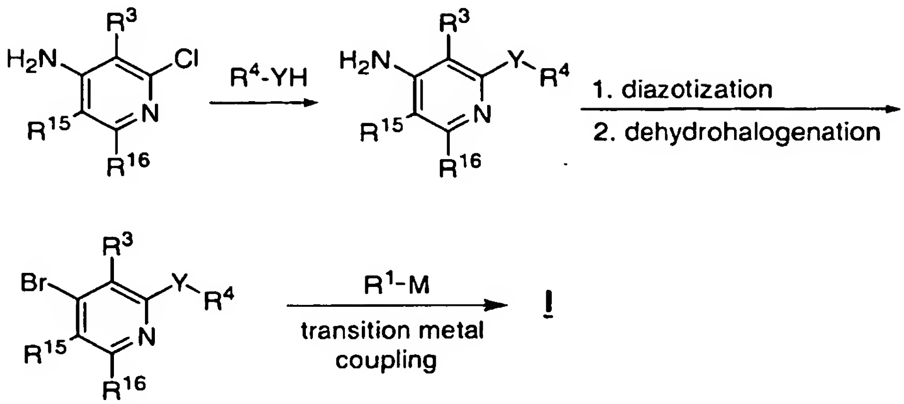
(d) Quinolin-3-yl- [4-(4-trifluoromethyl-phenyl)-pyridin-2-yl]-amine.

To an oven-dried 50 mL round-bottomed flask were added 2-chloro-4- (4-trifluoromethyl-phenyl)-pyridine (138 mg, 0.54 mmol) and 3-aminoquinoline (Aldrich Chemical Company) (93 mg, 0.64 mmol), followed by anhydrous toluene (45 mL). Nitrogen was bubbled through the above solution via a needle for 1h. Then palladium acetate (Aldrich Chemical Company) (18 mg, 0.08 mmol) and BINAP (Aldrich Chemical Company) (50 mg, 0.08 mmol) were added to the reaction in one portion, followed by sodium tert-butoxide (Aldrich Chemical Company) (145 mg, 1.5 mmol). The reaction mixture was heated at 90 °C overnight. After cooling to room temperature, the reaction mixture was taken up to ether, and washed with brine. The aqueous layer was extracted with ether (2x) and the combined ether layer was dried over Na_2SO_4 and concentrated. The residue was purified on a Biotage 40 S column (2.5:1 hexane:EtOAc) to give the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 366 (M+1). Mp: 207.4-207.5 °C.

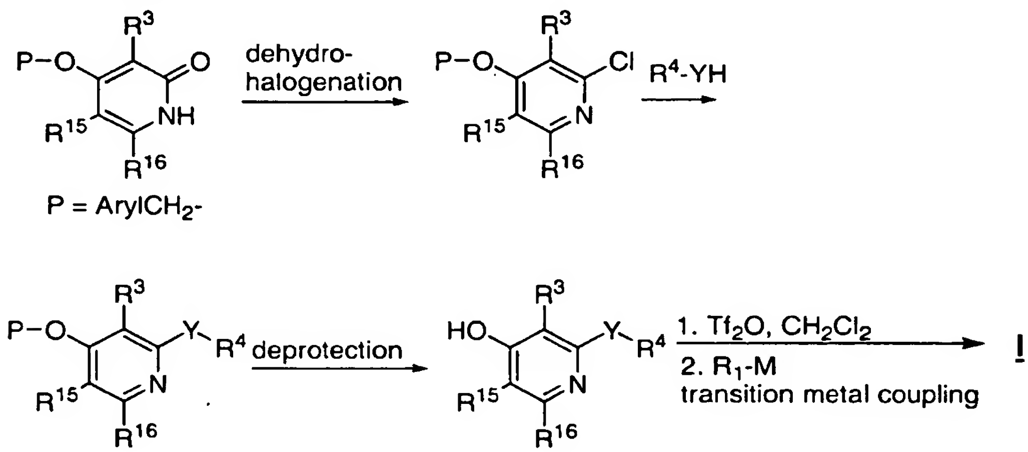
General Scheme III.a



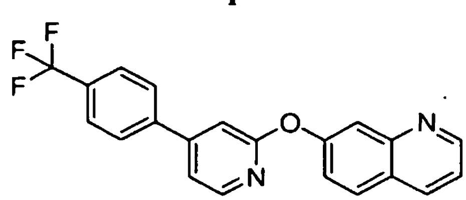
Scheme III.b



Scheme III.c



Example 134

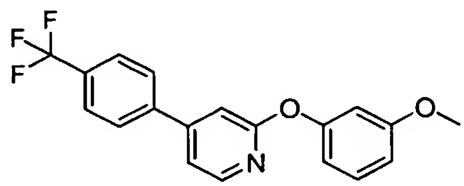


7-[4-(4-Trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinoline.

To an oven-dried, 50-mL, round-bottomed flask were added 7-hydroxyquinoline (Aldrich) (87 mg, 0.6 mmol) and DMF (1 mL). The solution was place under nitrogen, and NaH (24 mg, 0.6 mmol) was added in one portion. After stirring for 10 min, 2-chloro-4-(4-trifluoromethylphenyl) pyridine (Example 410 (c), 129 mg, 0.5 mmol) was added. The reaction mixture was heated in a 155 °C oil bath for

72 h. After cooling to room temperature, the reaction mixture was partitioned between EtOAc and brine. The aqueous layer was extracted with EtOAc and the combined organic layers were dried over Na_2SO_4, concentrated in vacuo. The crude material was purified on a Biotage 40 S column (3:1 hexanes: EtOAc) to give the title compound as an off-white solid. MS (ESI, pos. ion) *m/z*: 367 (M+1). Mp: 156.5-158.5 °C.

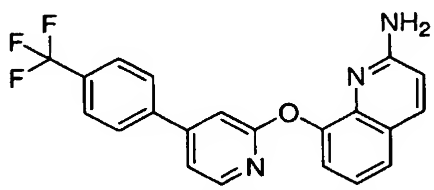
Example 135



2-(3-Methoxy-phenoxy)-4-(4-trifluoromethyl-phenyl)-pyridine.

This material was prepared according to the method described in Example 2 (d) using 2-chloro-4- (4-trifluoromethyl-phenyl)-pyridine (Example 410 (c), 129 mg, 0.5 mmol), 3-methoxyphenol (66 uL, 0.6 mmol), and sodium hydride (24 mg, 0.6 mmol) in DMF (1 mL). Purification on a Biotage 40S column (8:1 hexanes: EtOAc), provided the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 346 (M+1). Mp: 77.5- 79.6 °C.

Example 136

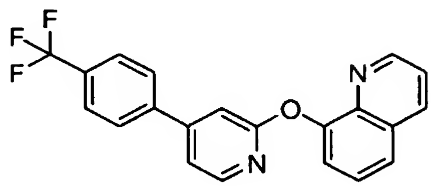


8-[4-(4-Trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinolin-2-ylamine.

A mixture of 2-azido-quinolin-8-ol (0.28 g, 1.5 mmol), 2-chloro-4- (4-trifluoromethyl-phenyl)-pyridine (Example 410 (c), 0.26 g, 1 mmol), and sodium hydride (64 mg, 1.6 mmol) in DMF (2 mL) was heated in a 180 °C oil bath for 48 h. The reaction mixture was then transferred to a 5-mL tube, and irradiated in the Microwave Smith Synthesizer at 250 °C for 10 min. EtOAc and brine were added, and the aqueous layer was extracted with EtOAc. Combined organic layers were dried over Na_2SO_4, filtered, and concentrated in vacuo. The compound was purified on a Biotage 40S column (98:2 dichloromethane: MeOH)

followed by recrystallization from EtOAc/hexanes to give the title compound as a light-yellow shiny crystal. MS (ESI, pos. ion) *m/z*: 382 (M+1). Mp: 196.5-199.5 °C. Anal. Calcd for $C_{21}H_{14}F_3N_3O$: C, 66.14; H, 3.70; N, 11.02. Found: C, 66.18; H, 3.69; N, 11.08.

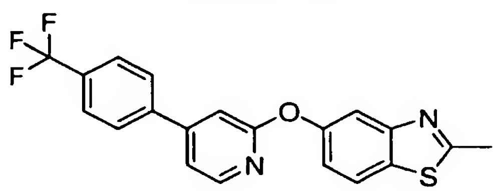
Example 137



8-[4-(4-Trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinoline.

This material was prepared according to the method described in Example 413 using 2-chloro-4- (4-trifluoromethyl-phenyl)-pyridine (Example 410 (c), 0.16 g, 0.6 mmol), 8-hydroxyquinoline (0.1 g, 0.7 mmol), sodium hydride (38 mg, 1.0 mmol) and copper (I) iodide (12 mg, 0.06 mmol) in DMF (3 mL). Purification on a Biotage 40S column (3:1 hexanes: EtOAc), provided the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 367 (M+1). Anal. Calcd for $C_{21}H_{13}F_3N_2O$: C, 68.85; H, 3.58; N, 7.65. Found: C, 68.88; H, 3.59; N, 7.51.

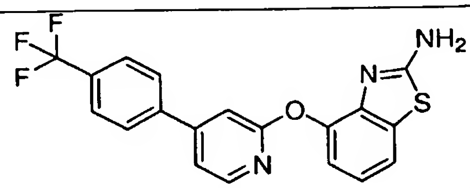
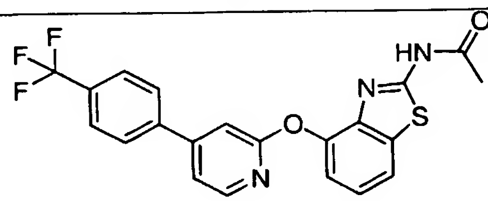
Example 138



2-Methyl-5-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-benzothiazole.

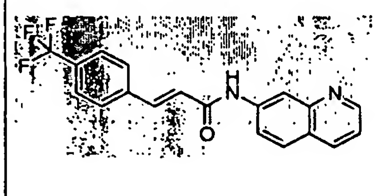
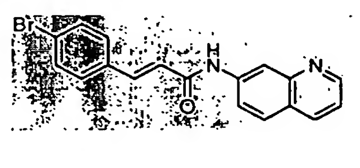
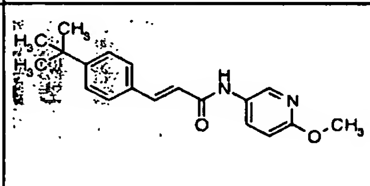
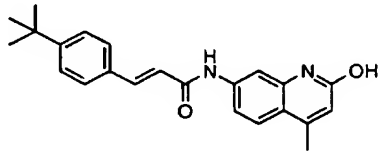
This material was prepared according to the method described in Example 413 using 2-chloro-4- (4-trifluoromethyl-phenyl)-pyridine (Example 410 (c), 0.16 g, 0.6 mmol), 2-methyl-5-benzothiazolol (0.12 g, 0.7 mmol), sodium hydride (38 mg, 1.0 mmol) and copper (I) iodide (12 mg, 0.06 mmol) in DMF (3 mL). Purification on a Biotage 40S column (3:1 hexanes: EtOAc), provided the title compound as a white solid. MS (ESI, pos. ion) *m/z*: 367 (M+1). Mp: 160.5-163.5 °C. Anal. Calcd for $C_{20}H_{13}F_3N_2OS$. 0.25 H_2O: C, 61.45; H, 3.48; N, 7.17; S, 8.20. Found: C, 61.45; H, 3.39; N, 7.17; S, 8.31.

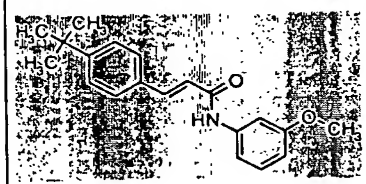
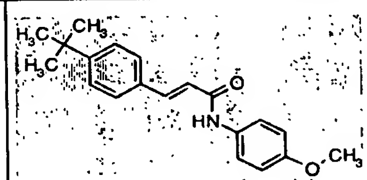
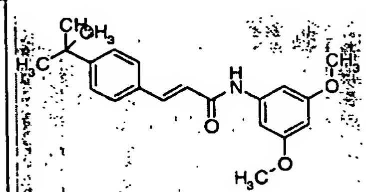
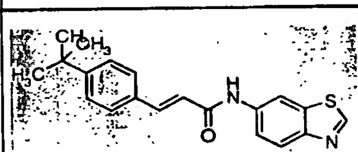
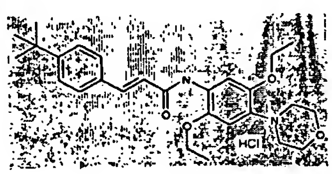
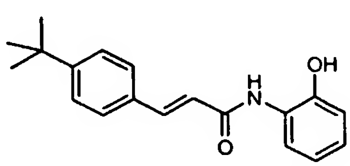
Table B. The following compounds were prepared according to General Schemes III.a, III.b and III.c:

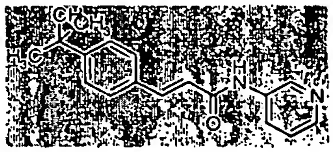
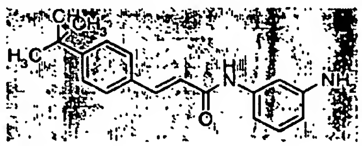
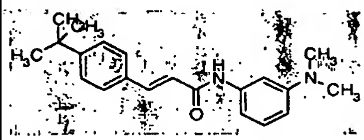
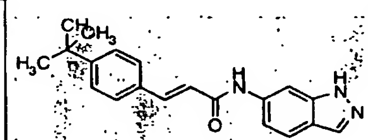
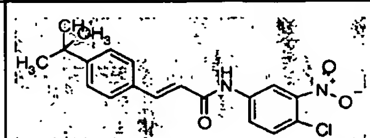
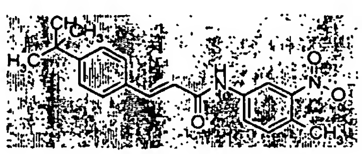
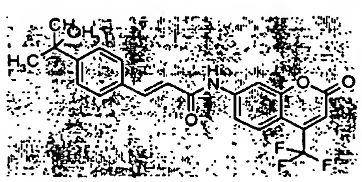
Example	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
139		388 (M+1)	246.3-247.5
140		428 (M-1) 430 (M+1)	

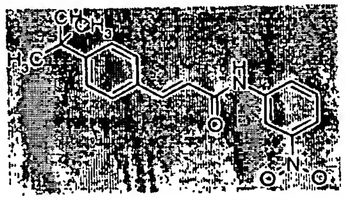
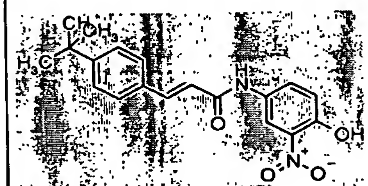
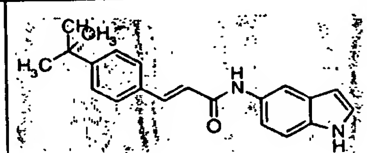
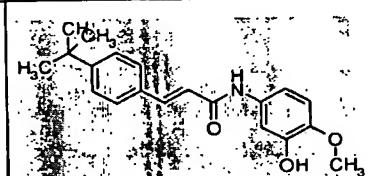
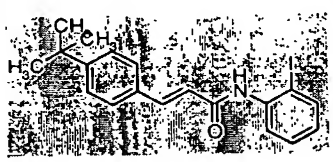
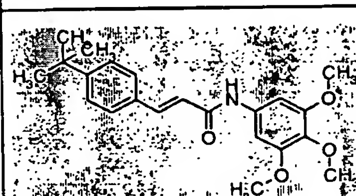
Additional Examples

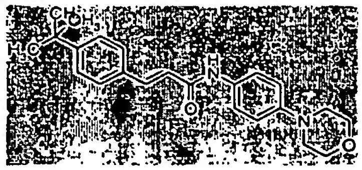
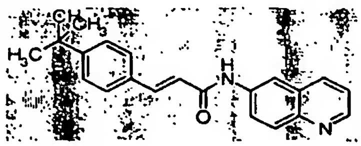
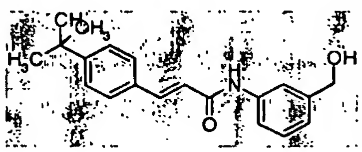
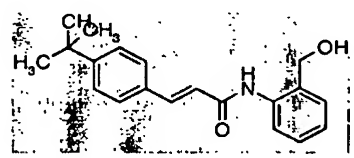
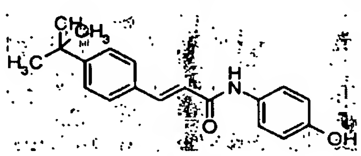
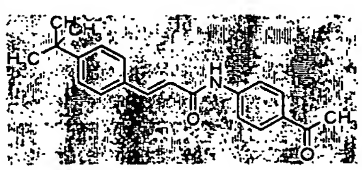
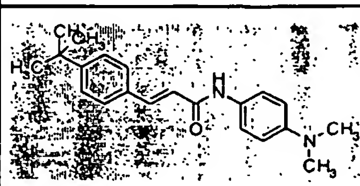
Following the procedures described above, or with slight modifications thereof, and following procedures familiar to one of ordinary skill in the art, the following examples were prepared from commercially available reagents:

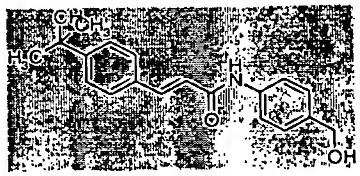
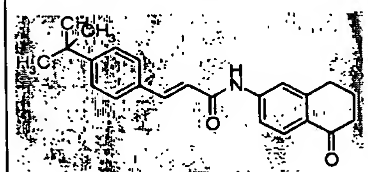
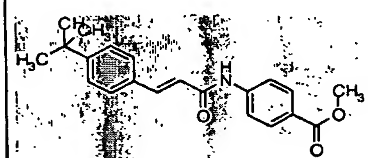
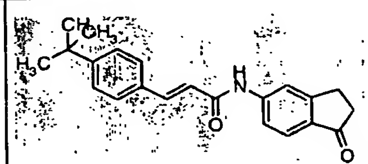
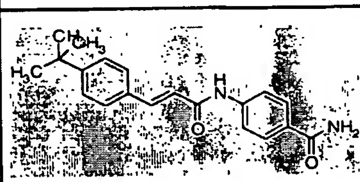
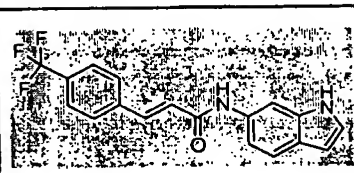
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
142		244	343 (M+1)
143		231	352, 354 (M, M+2)
144		159	311 (M+1)
145		>300	361 (M+1)

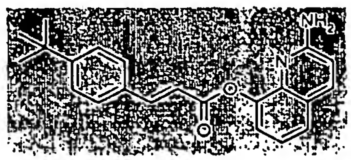
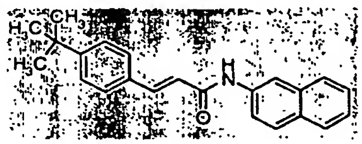
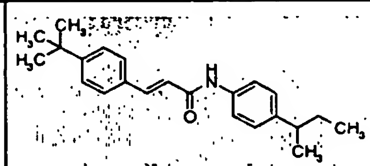
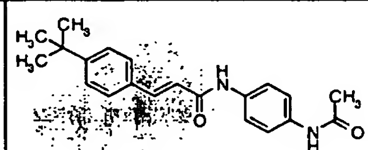
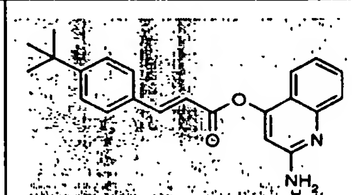
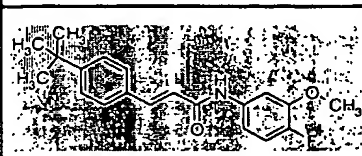
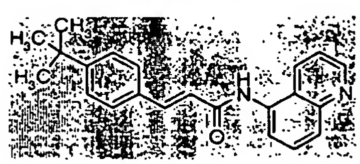
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
146		59-61	310 (M+1)
147		174-175	310 (M+1)
148		97-102	340 (M+1)
149		148-152	337 (M+1)
150		233-237	453 (M+1)
151		oil	296 (M+1)

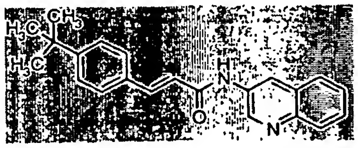
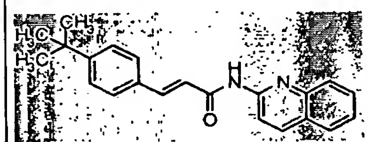
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
152		106-108	281 (M+1)
153		98-102	295 (M+1)
154		171-173	323 (M+1)
155		257	320 (M+1)
156		187-190	359 (M+1)
157		203	339 (M+1)
158		244-248	416 (M+1)

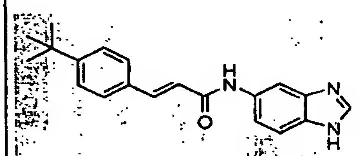
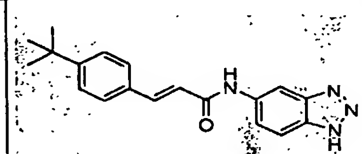
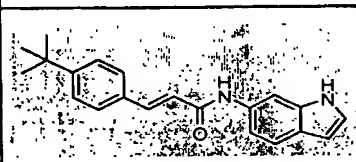
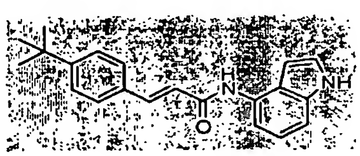
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
159		204	325 (M+1)
160		191	341 (M+1)
161		thin film	319 (M+1)
162		173	326 (M+1)
163		152	406 (M+1)
164		193	370 (M+1)

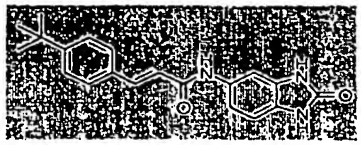
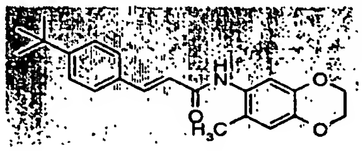
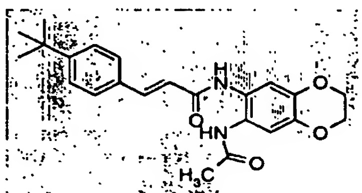
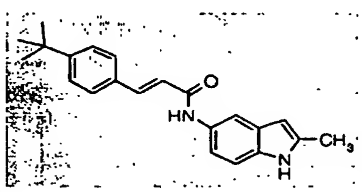
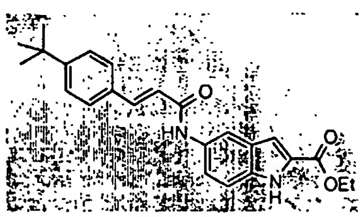
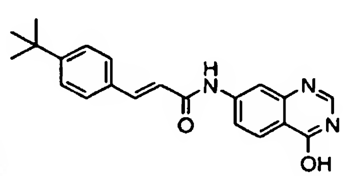
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
165		249	365 (M+1)
166		193	331 (M+1)
167		149	310 (M+1)
168		173	310 (M+1)
169		218	296 (M+1)
170		195	322 (M+1)
171		223	323 (M+1)

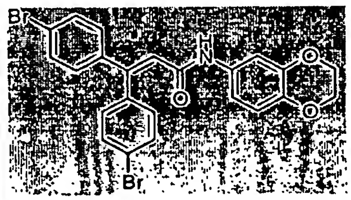
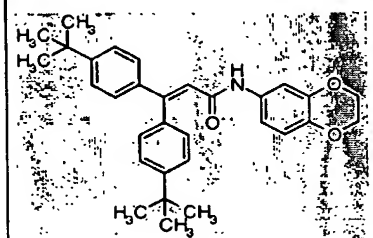
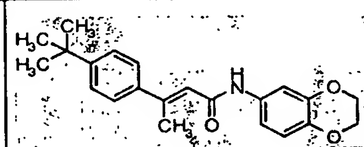
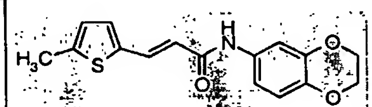
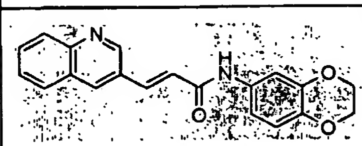
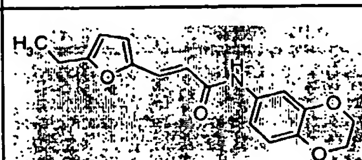
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
172		168	310 (M+1)
173		205	348 (M+1)
174		161	338 (M+1)
175		212	334 (M+1)
176		263	323 (M+1)
177		239	331 (M+1)

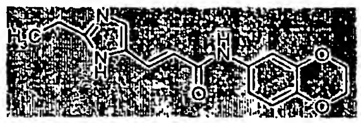
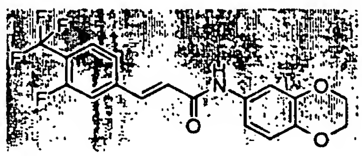
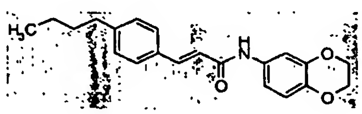
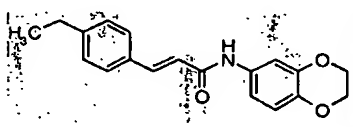
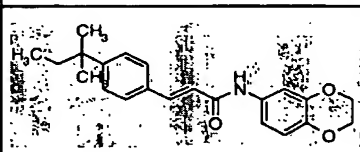
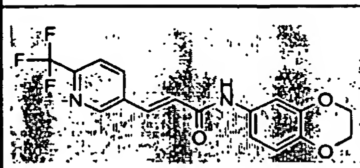
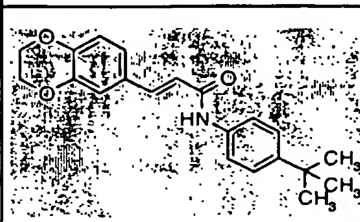
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
178		167	347 (M+1)
179		172	330 (M+1)
180		154	336 (M+1)
181		281	337 (M+1)
182		154	347 (M+1)
183		105	328 (M+1)
184		165	329 (M-1)

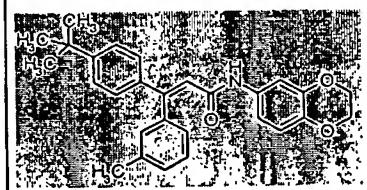
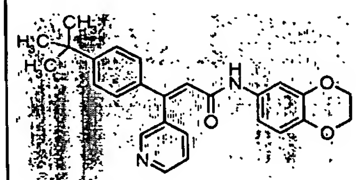
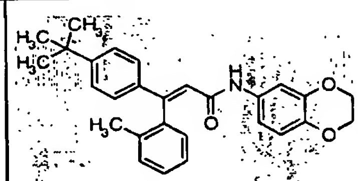
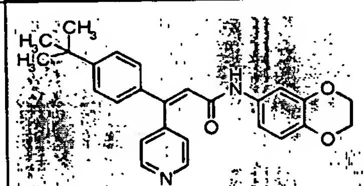
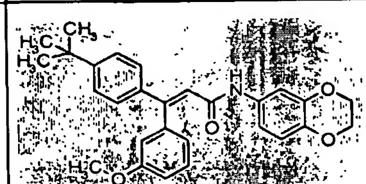
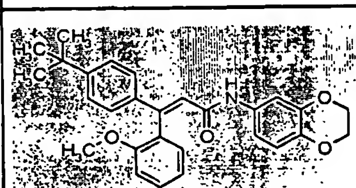
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
185		270	331 (M+1)
186		68	331 (M+1)

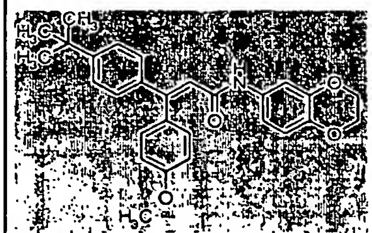
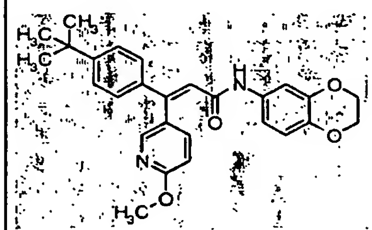
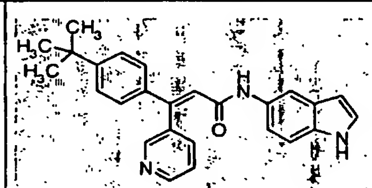
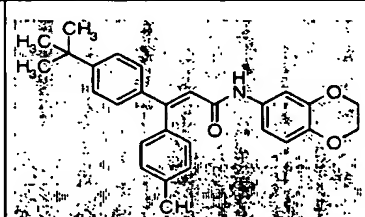
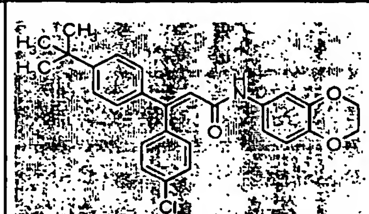
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
187		261	320 (M+1)
188		277	321 (M+1)
189		194	319 (M+1)
190		101	319 (M+1)

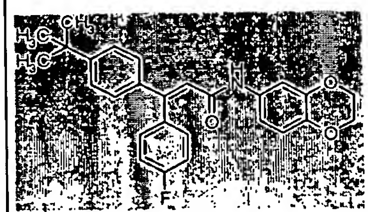
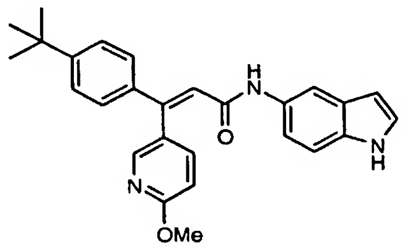
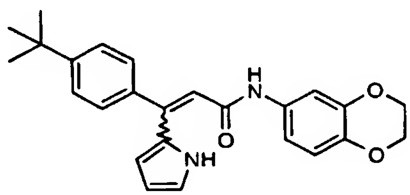
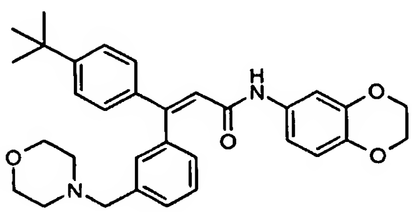
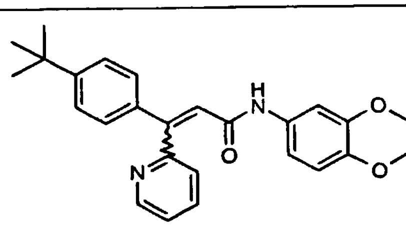
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
200		258	336 (M+1)
201		178	352 (M+1)
202		196	395 (M+1)
203		222	333 (M+1)
204		218	391 (M+1)
205		296-298	348 (M+1)

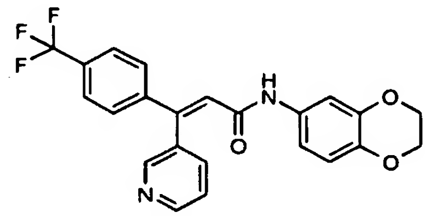
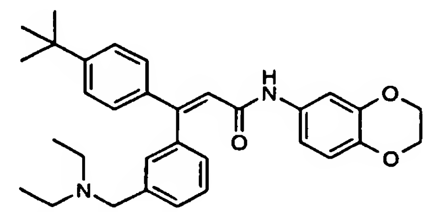
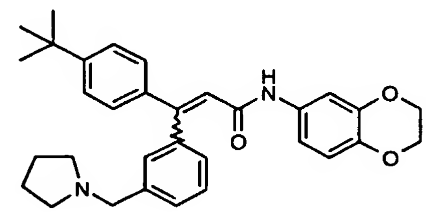
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
206		189	515 (M)
207		116-119	470 (M+1)
208		186	352 (M+1)
209		162-163	302 (M+1)
210		231-232	333 (M+1)
211		42-48	300 (M+1)

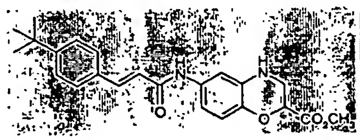
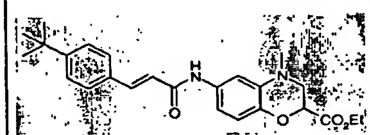
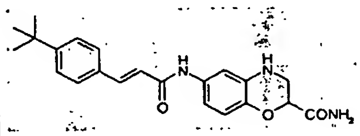
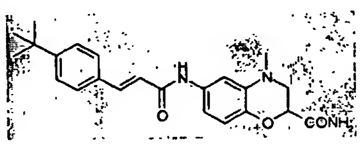
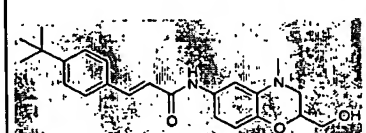
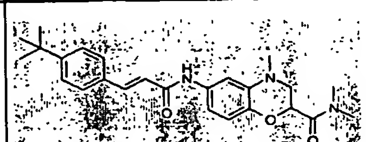
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
212		229-230	300 (M+1)
213		200-202	368 (M+1)
214		120	338 (M+1)
215		119	310 (M+1)
216		69	352 (M+1)
217		amorphous glass	351 (M+1)
218		84-90	338 (M+1)

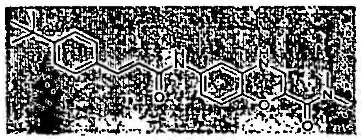
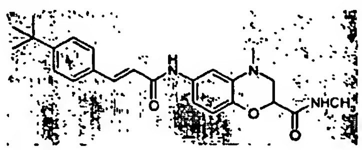
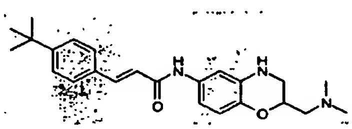
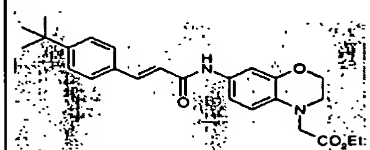
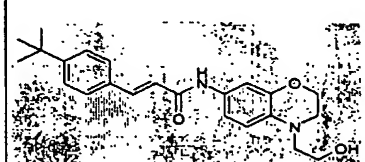
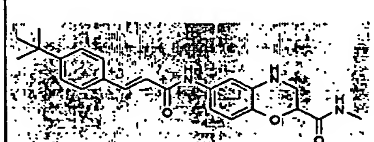
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
219		64-71	428 (M+1)
220		100-104	415 (M+1)
221		91-93	428 (M+1)
222		205-206	415 (M+1)
223		78-80	444 (M+1)
224		89-93	444 (M+1)

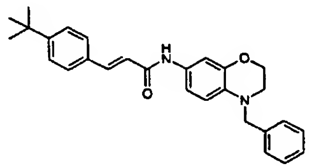
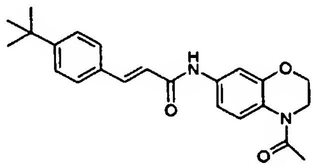
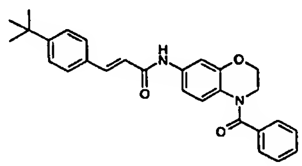
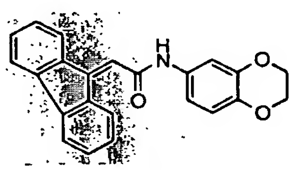
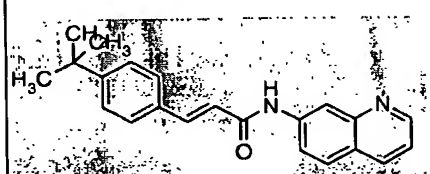
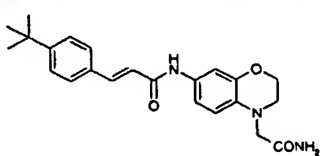
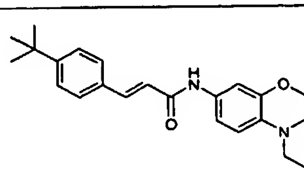
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
225		148-150	444 (M+1)
226		92-94	445 (M+1)
227		177-180	396 (M+1)
228		138-141	428 (M+1)
229		155	448 (M+1)

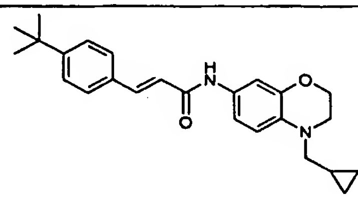
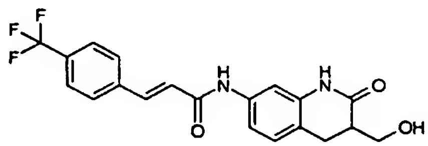
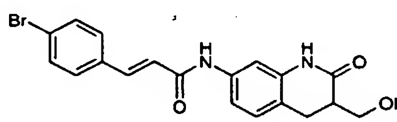
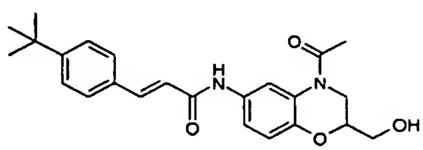
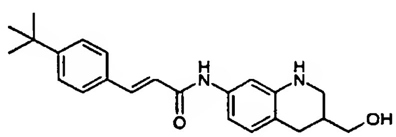
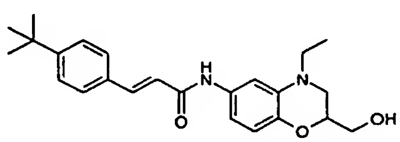
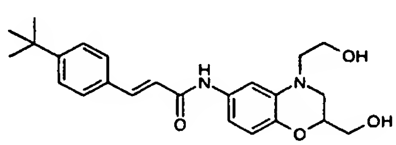
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
230		168	432 (M+1)
231		121-124	426 (M+1)
232			403 (M+1)
233		87	513 (M+1)
234			415 (M+1)

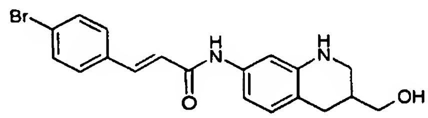
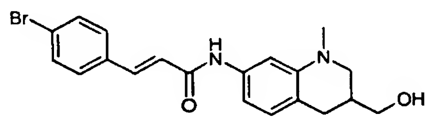
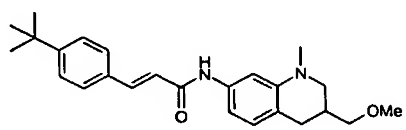
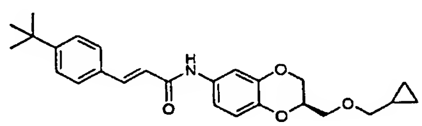
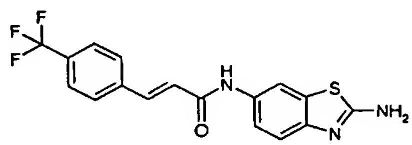
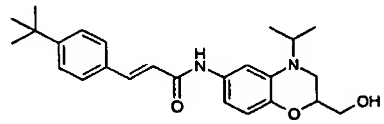
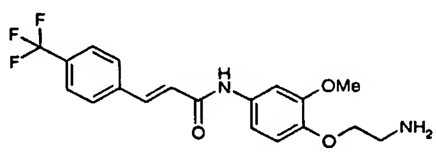
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
235		amorphous	427 (M+1)
236		56	499 (M+1)
237			497 (M+1)

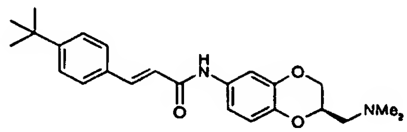
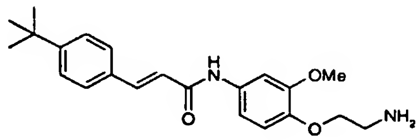
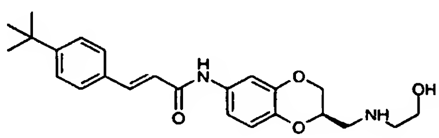
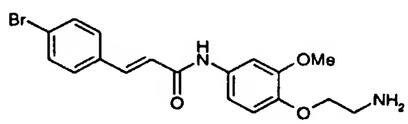
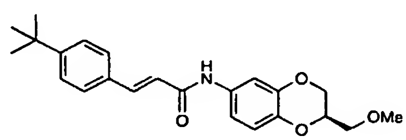
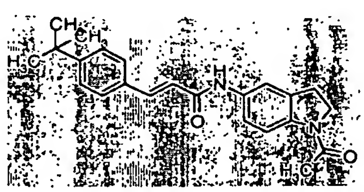
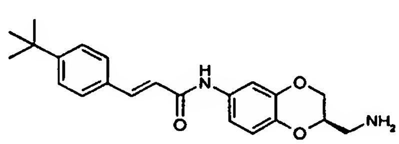
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
238		207-208	395 (M+1)
239		188-189	423 (M+1)
240		198-199	380 (M+1)
241		201-203	394 (M+1)
242		171-173	381 (M+1)
243		118-120	422 (M+1)

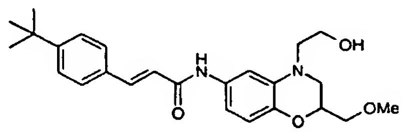
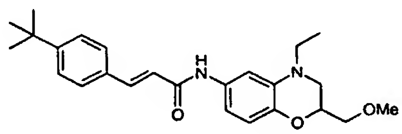
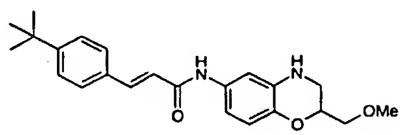
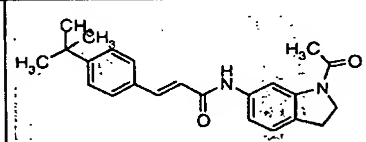
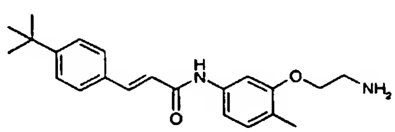
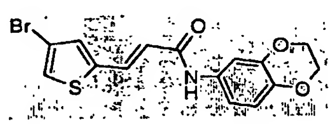
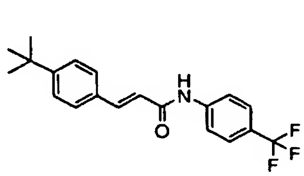
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
244		101-103	408 (M+1)
245		126-128	408 (M+1)
246		185-186	394 (M+1)
247		182-184	423 (M+1)
248		194-196	381 (M+1)
249		206-208	394 (M+1)

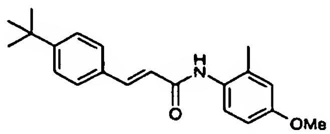
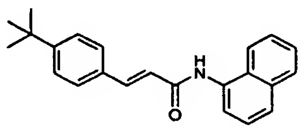
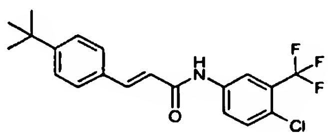
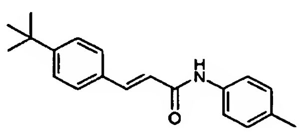
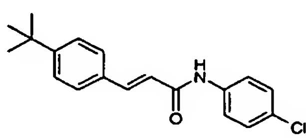
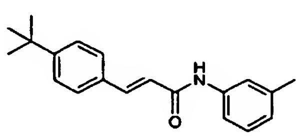
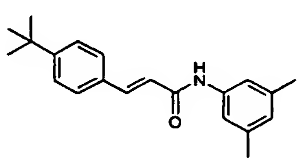
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
250		200-201	427 (M+1)
251		199-200	379 (M+1)
252		236-237	441 (M+1)
253		169	356 (M+1)
254		256-258	331 (M+1)
255		264-266	394 (M+1)
256		102-103	365 (M+1)

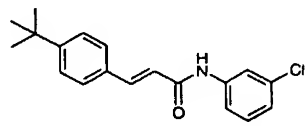
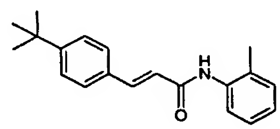
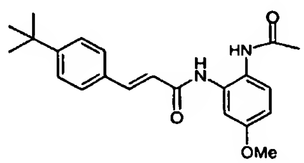
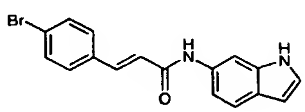
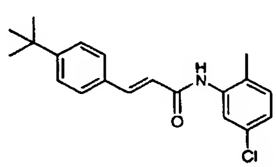
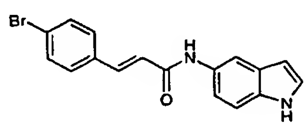
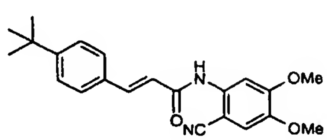
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
257		137-138	391 (M+1)
258		198-200	391 (M+1)
259		171-173	402 (M+1)
260		158-160	409 (M+1)
261		168-170	365 (M+1)
262		179-180	395 (M+1)
263		117-119	411 (M+1)

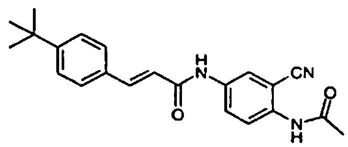
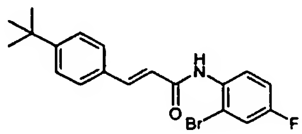
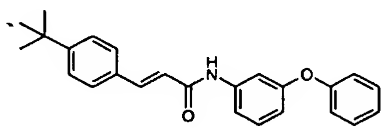
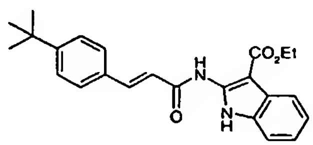
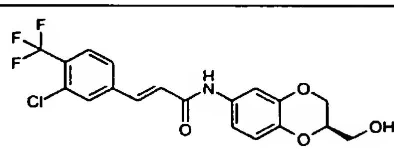
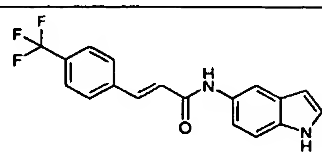
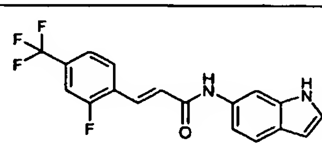
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
264		187-189	388 (M+1)
265		154-157	402 (M+1)
266		160-161	395 (M+1)
267		152-153	422 (M+1)
268		186-188	364 (M+1)
269		134-135	409 (M+1)
270		182-185	381 (M+1)

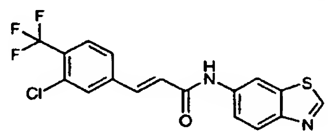
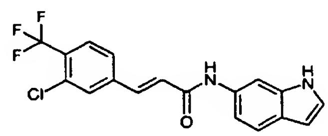
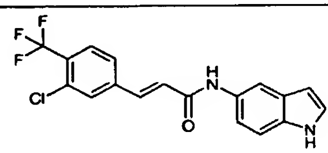
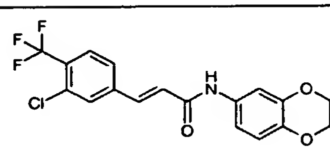
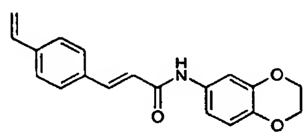
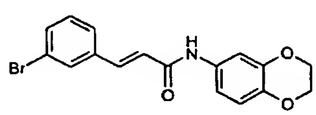
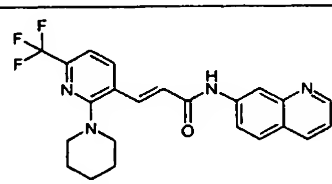
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
271		171-173	395 (M+1)
272		101-105	369 (M+1)
273		176-178	411 (M+1)
274		196-199	392 (M+1)
275		146-148	382 (M+1)
276		231	363 (M+1)
277		161-162	367 (M+1)

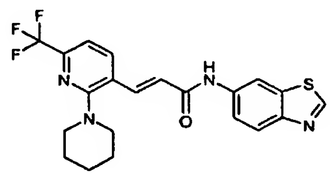
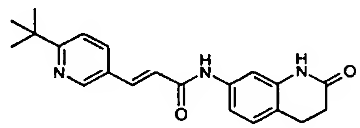
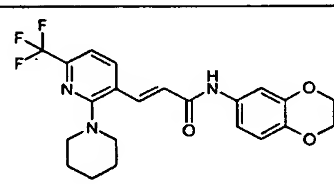
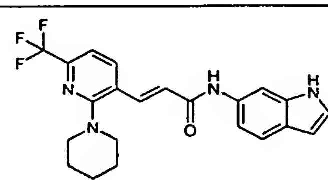
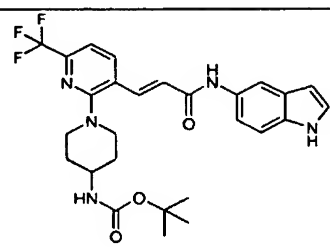
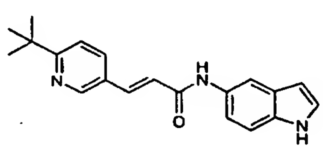
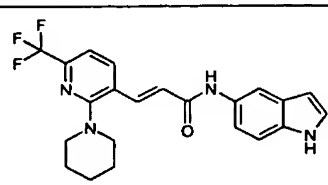
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
278		108-110	425 (M+1)
279		186-187	409 (M+1)
280		160-162	381 (M+1)
281		181	363 (M+1)
282		amorphous	353 (M+1)
283		(oil)	366 (M)
284			348 (M+1)

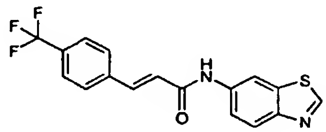
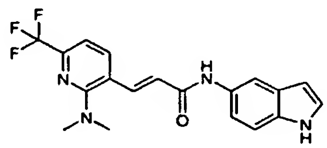
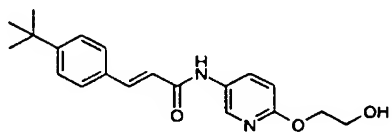
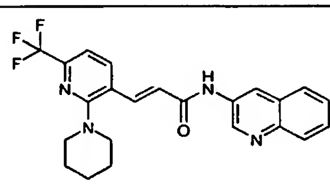
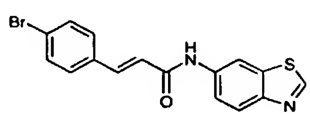
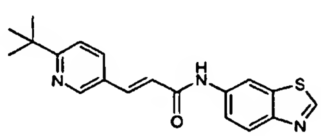
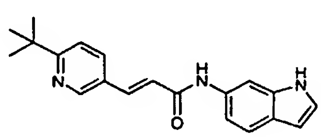
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
285			324 (M+1)
286			330 (M+1)
287			382 (M+1)
288			294 (M+1)
289			314 (M+1)
290			294 (M+1)
291			308 (M+1)

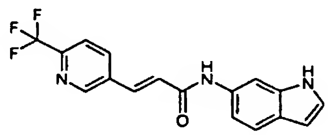
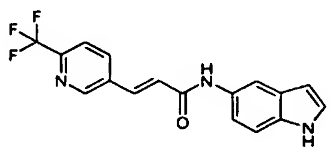
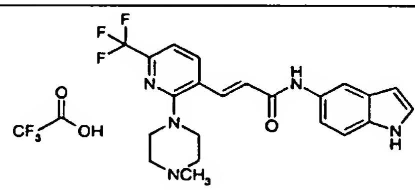
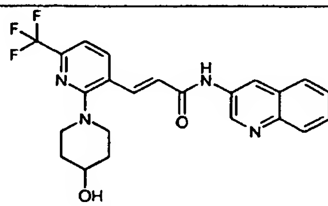
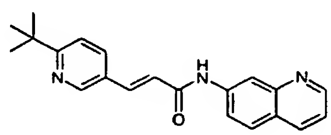
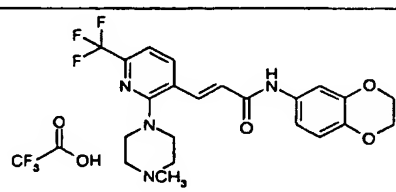
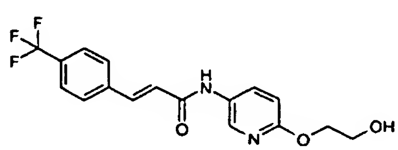
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
292			314 (M+1)
293			294 (M+1)
294			367 (M+1)
295		246-247	341 (M)
296			328 (M+1)
297		233-235	341 (M)
298			365 (M+1)

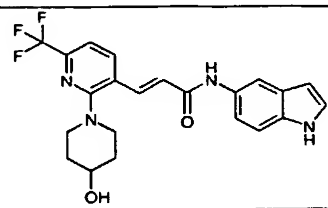
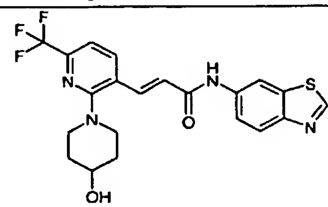
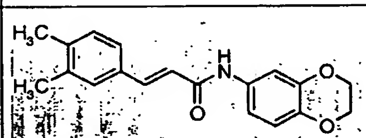
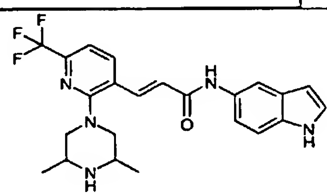
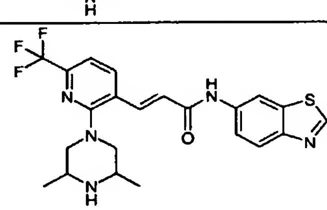
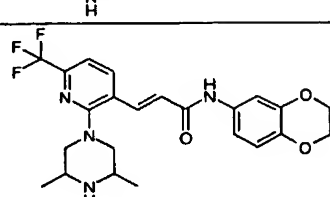
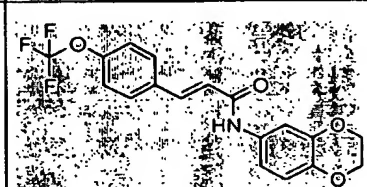
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
299			362 (M+1)
300			376 (M)
301			372 (M+1)
302		186-187	391 (M+1)
303		224-226	414 (M+1)
304		231-232	331 (M+1)
305		219-220	349 (M+1)

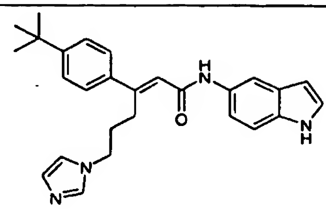
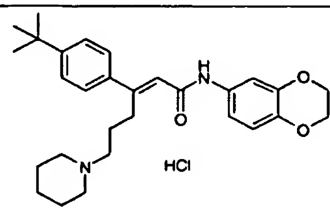
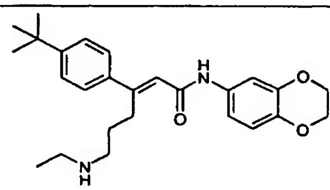
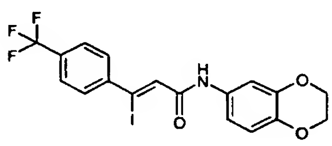
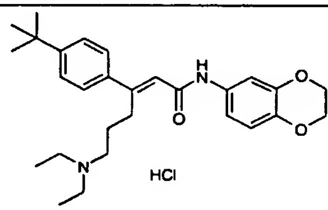
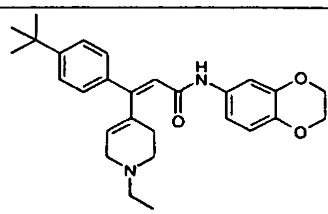
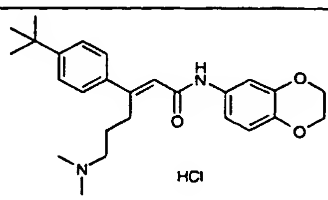
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
306		231-232	383 (M+1)
307		203-204	365 (M+1)
308		177-179	365 (M+1)
309		226-227	384 (M+1)
310		Amorphous	308 (M+1)
311		150	360 (M)
312		211	427 (M+1)

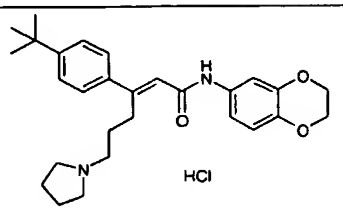
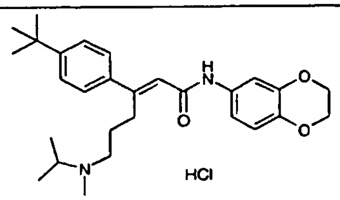
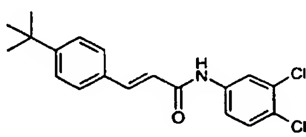
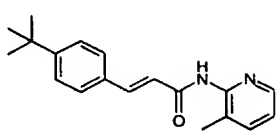
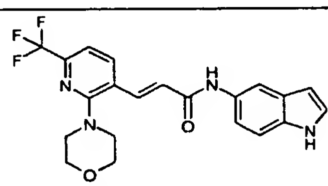
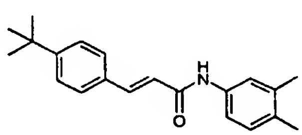
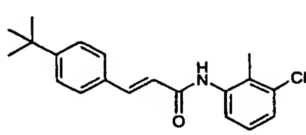
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
313		78	433 (M+1)
314		286	350 (M+1)
315		Amorphous	434 (M+1)
316		226	415 (M+1)
317		219	530 (M+1)
318		Amorphous	320 (M+1)
319		Amorphous	415 (M+1)

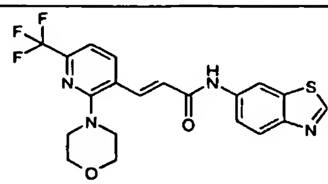
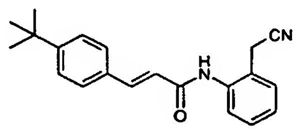
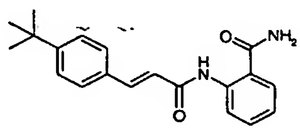
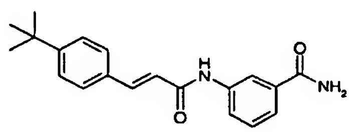
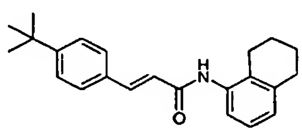
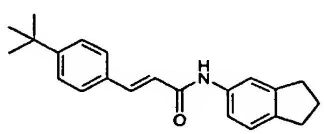
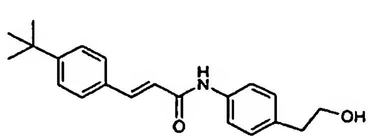
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
320		211	349 (M+1)
321		Amorphous	375 (M+1)
322		Amorphous	341 (M+1)
323		Amorphous	427 (M+1)
324		225	360 (M+1)
325		Amorphous	338 (M+1)
326		275	320 (M+1)

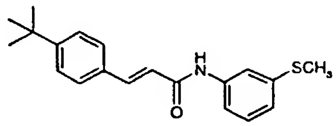
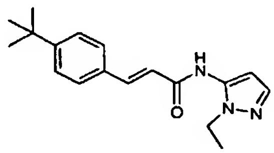
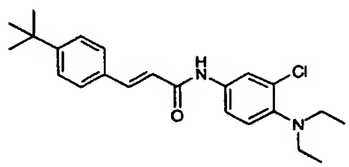
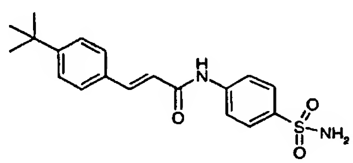
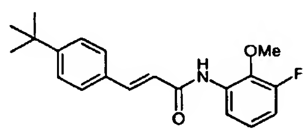
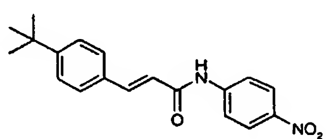
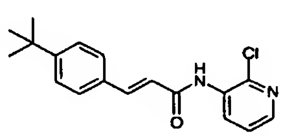
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
327		282	332 (M+1)
328		209	332 (M+1)
329		Amorphous	430 (M+1)
330		197	443 (M+1)
331		Amorphous	332 (M+1)
332		Amorphous	448 (M)
333		202	353 (M+1)

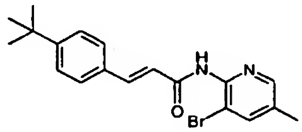
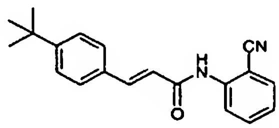
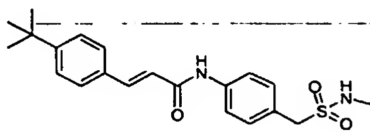
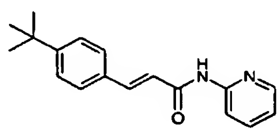
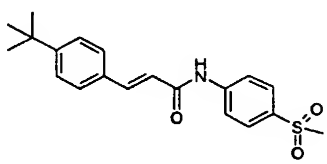
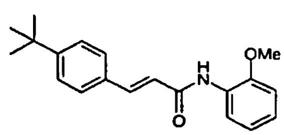
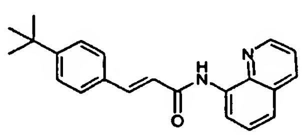
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
334		229	431 (M+1)
335		97	449 (M+1)
336		121	309 (M)
337		Amorphous	444 (M+1)
338		Amorphous	462 (M+1)
339		Amorphous	463 (M+1)
340		163	366 (M+1)

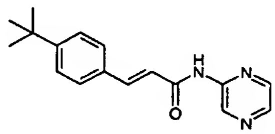
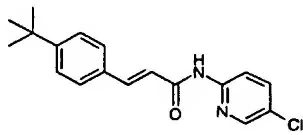
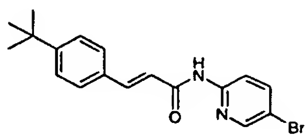
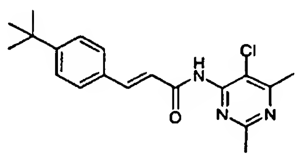
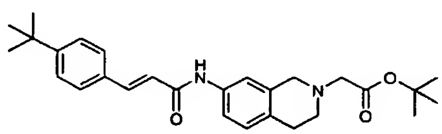
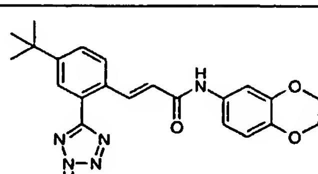
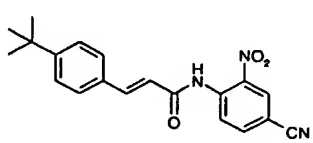
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
341		237-240	427 (M+1)
342		276-278	463 (M+1)
343		amorphous	423 (M+1)
344		202-204	476 (M+1)
345		214-218	451 (M+1)
346		amorphous	447 (M+1)
347		201-205	423 (M+1)

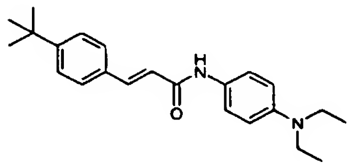
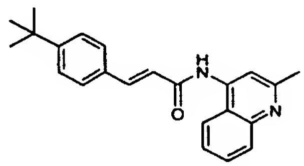
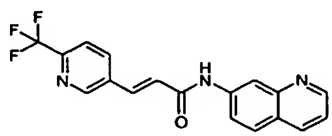
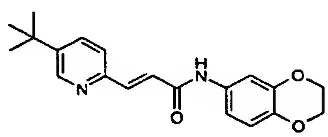
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
348		263-269	449 (M+1)
349		273-275	451 (M+1)
350			348 (M+1)
351			295 (M+1)
352		amorphous	417 (M+1)
353			308 (M+1)
354			328 (M+1)

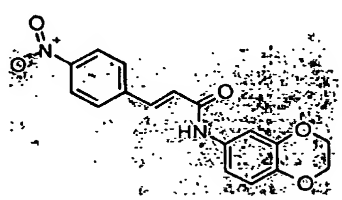
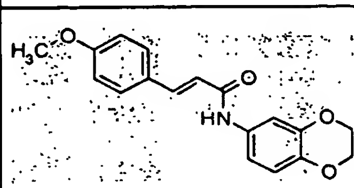
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
355		amorphous	435 (M+1)
356			319 (M+1)
357			323 (M+1)
358			323 (M+1)
359			334 (M+1)
360			320 (M+1)
361			324 (M+1)

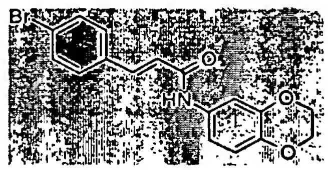
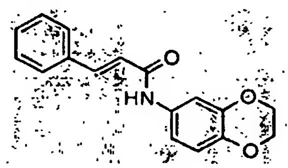
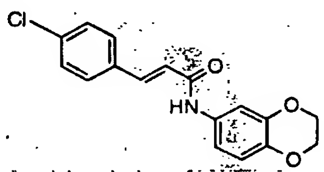
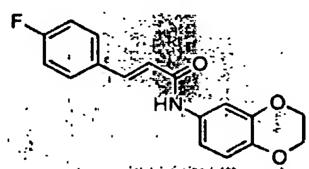
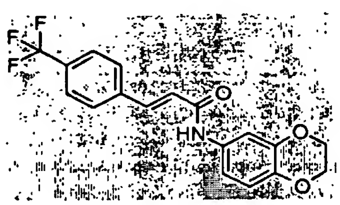
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
362			294 (M+1)
363			298 (M+1)
364			385 (M+1)
365			359 (M+1)
366			328 (M+1)
367			325 (M+1)
368			315 (M+1)

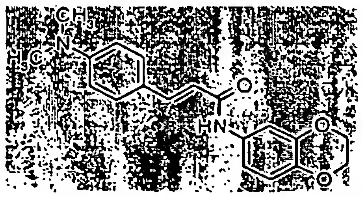
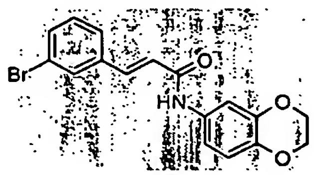
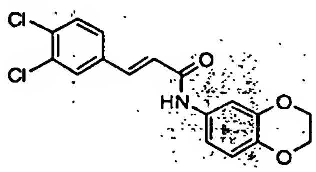
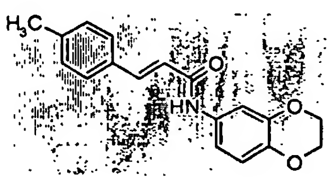
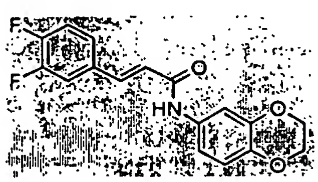
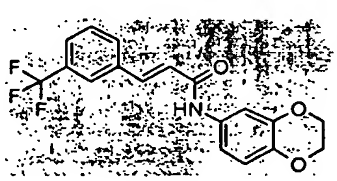
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
369			374 (M+1)
370			305 (M+1)
371			387 (M+1)
372			281 (M+1)
373			358 (M+1)
374			310 (M+1)
375			331 (M+1)

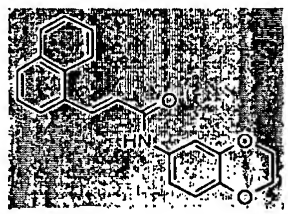
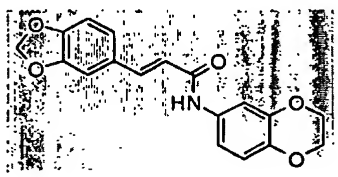
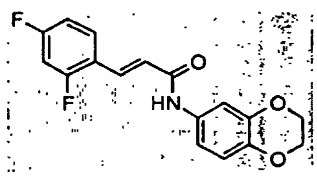
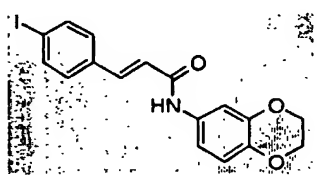
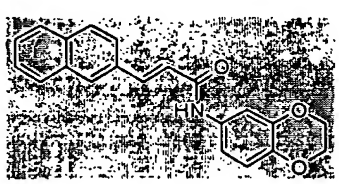
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
376			282 (M+1)
377			315 (M+1)
378			360 (M+1)
379			344 (M+1)
380		amorphous	449 (M+1)
381		amorphous	401 (M+1)
382			350 (M+1)

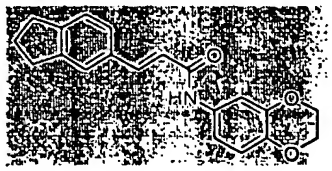
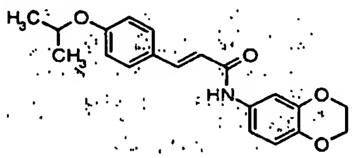
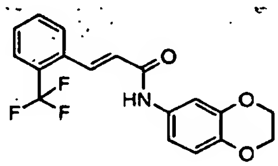
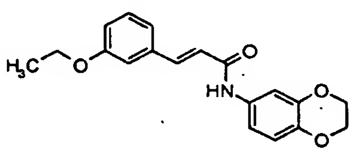
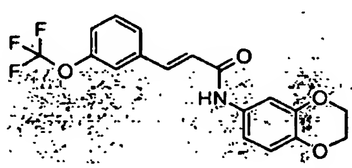
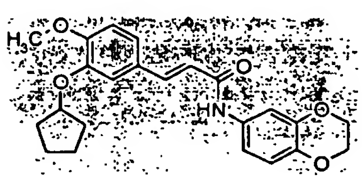
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
383			351 (M+1)
384			345 (M+1)
385			344 (M+1)
386			339 (M+1)

Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
387		247-248	327 (M+1)
388		179-180	312 (M+1)

Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
389		179-182	360, 362 (M, M+2)
390		182-183	282 (M+1)
391		187-188	316 (M+1)
392		195-196	300 (M+1)
393		201-202	350 (M+1)

Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
394		214-216	325 (M+1)
395		150	360 (M+1)
396		184-189	350 (M+1)
397		173-175	296 (M+1)
398		160-165	318 (M+1)
399		200	350 (M+1)

Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
400		203-207	332 (M+1)
401		155-158	326 (M+1)
402		181-182	318 (M+1)
403		196	408 (M+1)
404		185-186	332 (M+1)

Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) m/z
405		(oil)	322 (M+1)
406		188	340 (M+1)
407		176	350 (M+1)
408		(oil)	326 (M+1)
409		129	366 (M+1)
410		202	396 (M+1)

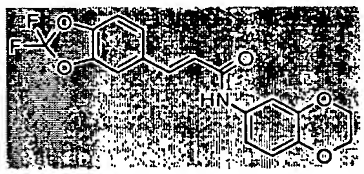
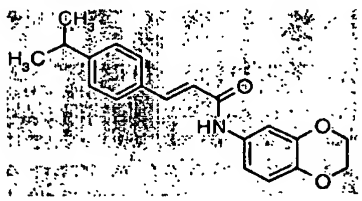
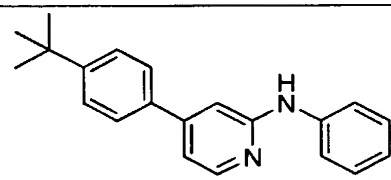
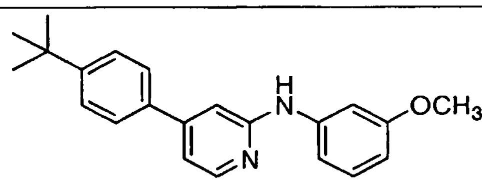
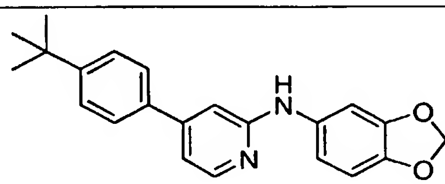
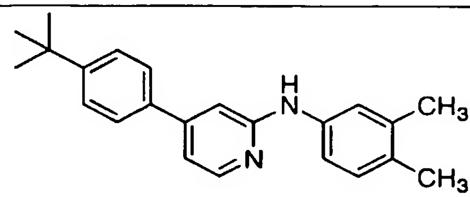
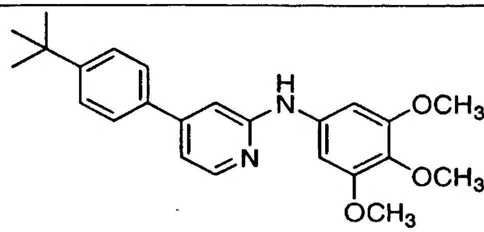
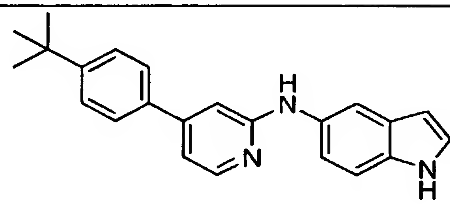
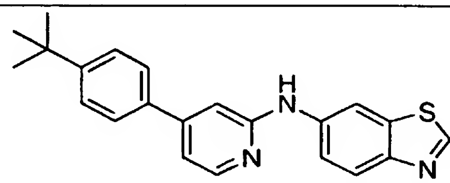
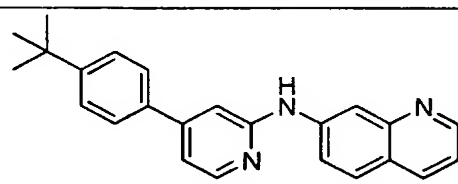
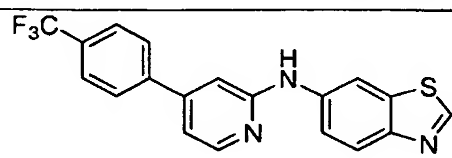
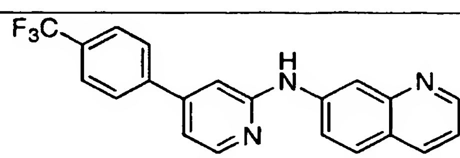
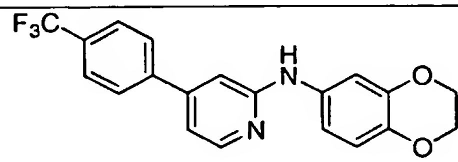
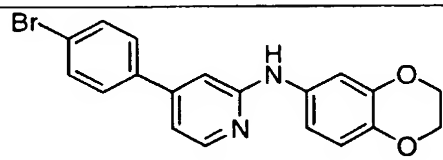
Example number	Structure	Melting Point (°C)	Mass Spec. (ESI) *m/z*
411		191	362 (M+1)
412		165	324 (M+1)

Table. The following compounds were prepared according to General Schemes **I**, **II** or **III**:

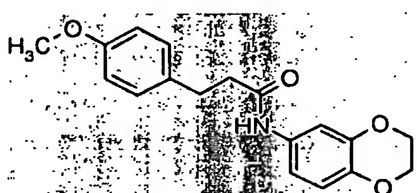
Example number	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
413		303 (M+1)	157
414		333 (M+1)	amorphous
415		347 (M+1)	156

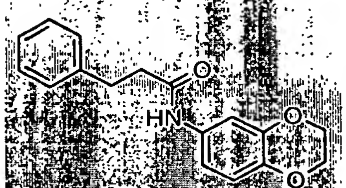
Example number	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
416		331 (M+1)	133
417		393 (M+1)	amorphous
418		342 (M+1)	106
419		360 (M+1)	154
420		354 (M+1)	214
421		372 (M+1)	203
422		366 (M+1)	206

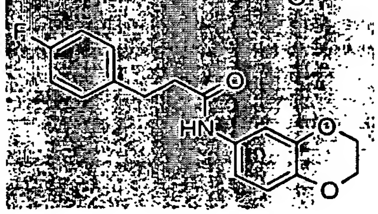
Example number	Structure	MS (ESI, pos. ion) *m/z*	Melting Point °C
423		373 (M+1)	114
424		383, 385 (M, M+2)	124

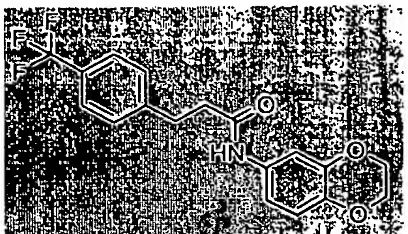
Additional Examples

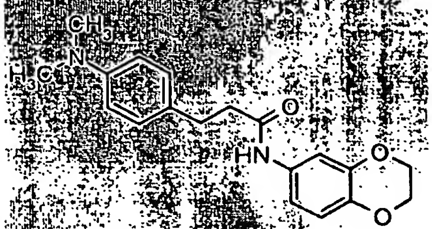
Following the procedures described above, and applying the procedure in Example 109 to the cinnamides exemplified, or with slight modifications thereof, and following procedures familiar to one of ordinary skill in the art, the following examples may be prepared from commercially available reagents:

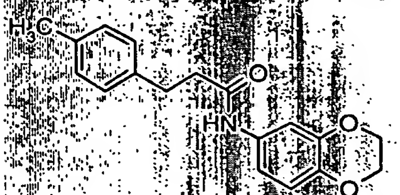


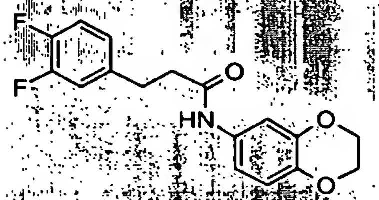


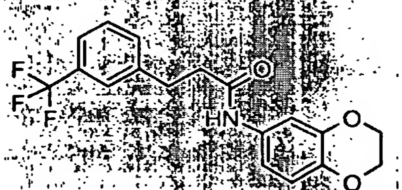


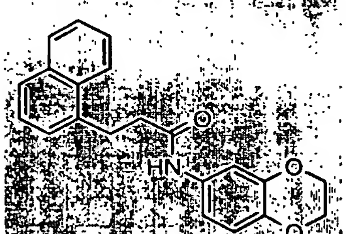


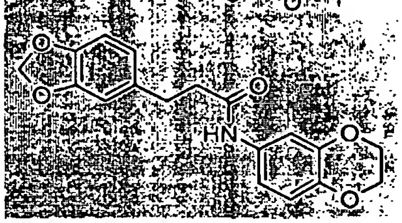


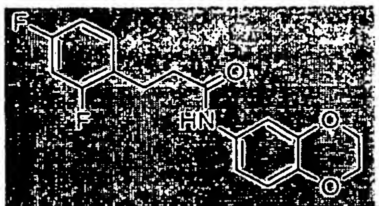


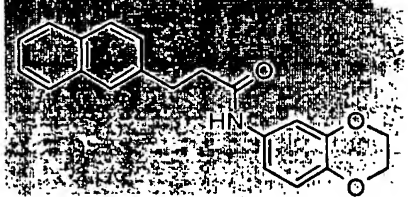


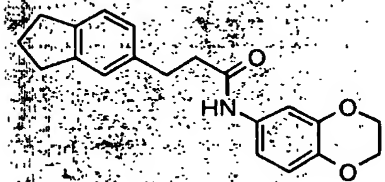


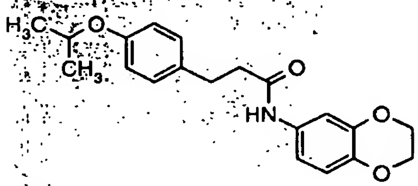


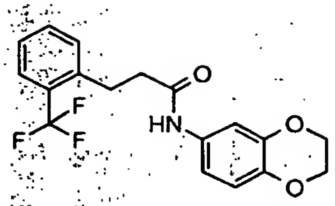


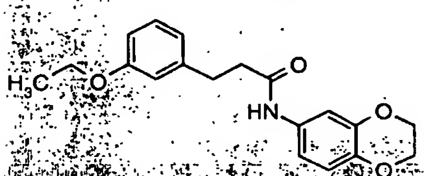


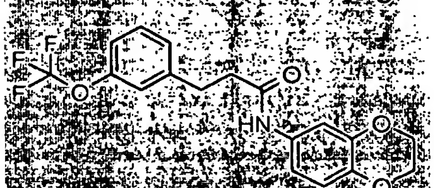


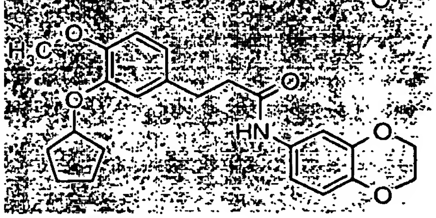


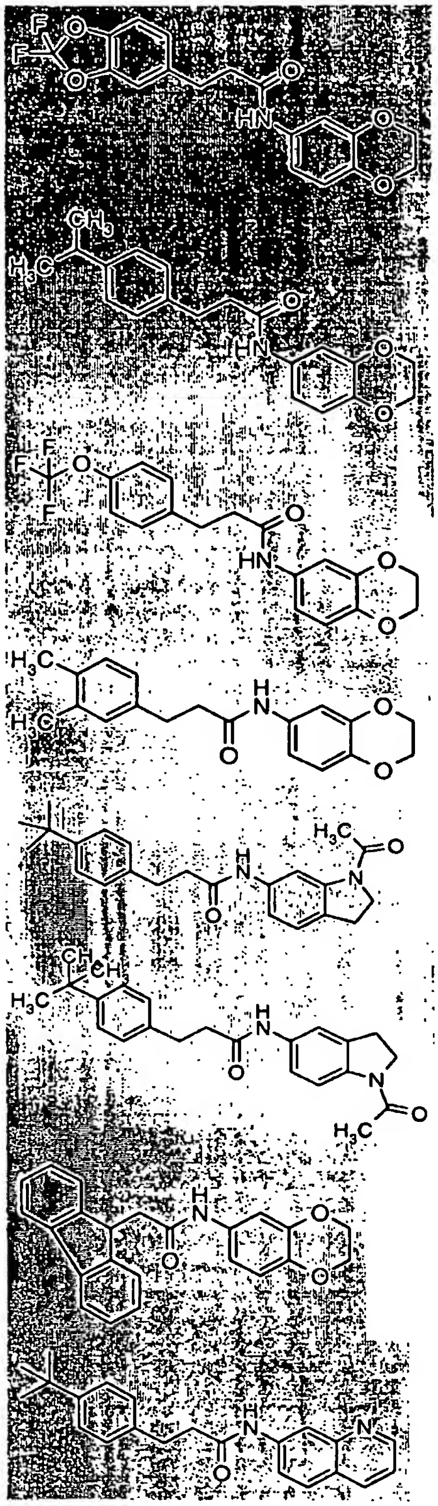


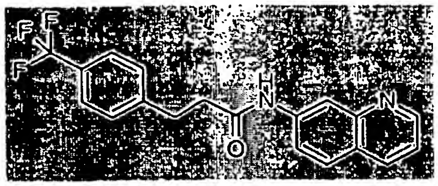


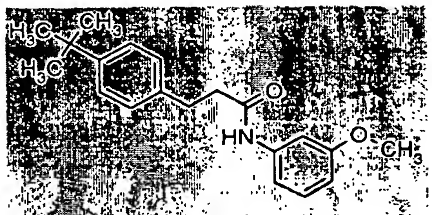


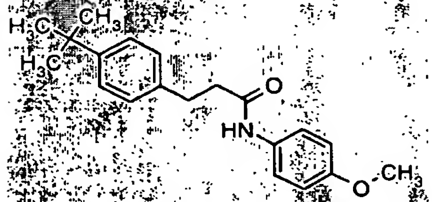


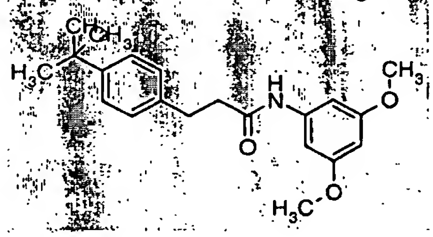


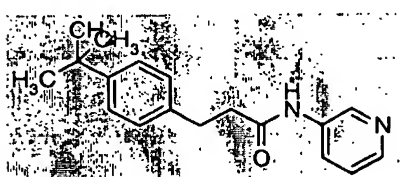


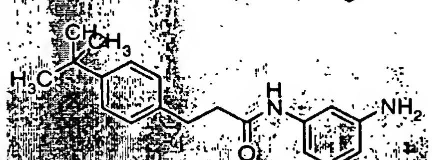


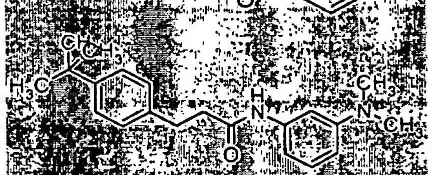


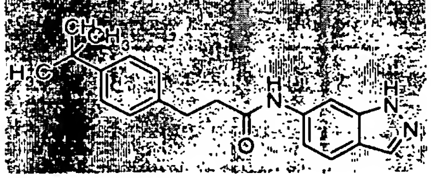


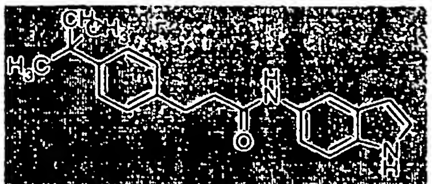


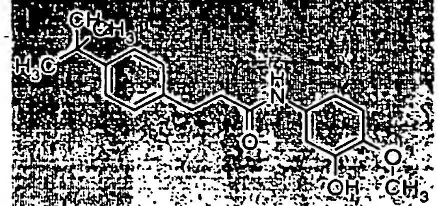


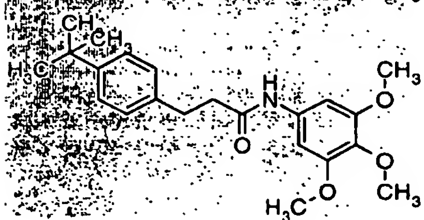


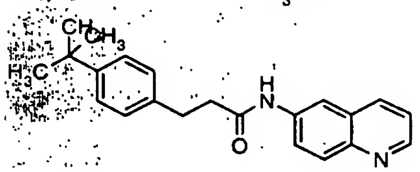


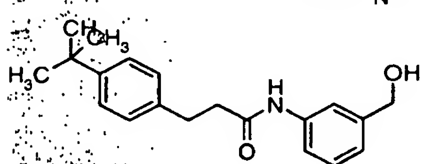


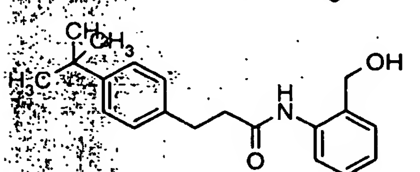


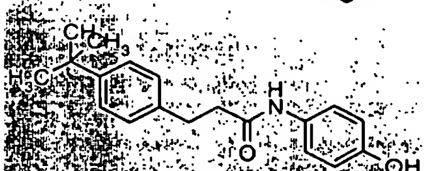


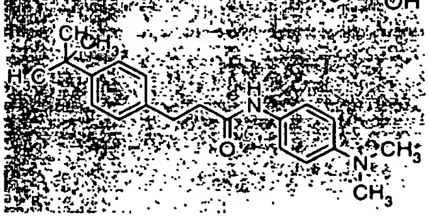


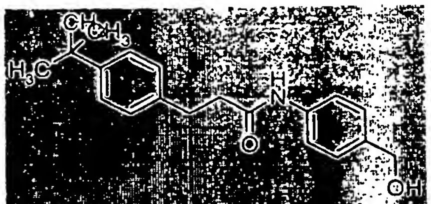


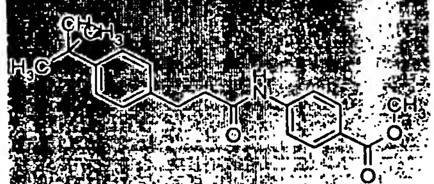


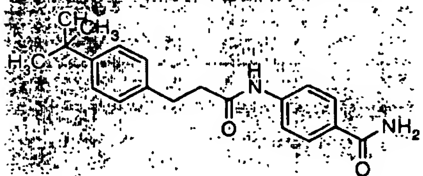


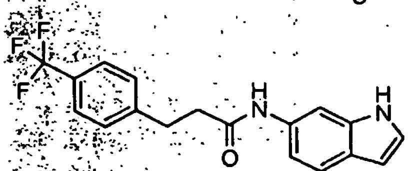


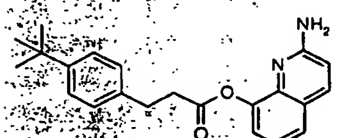


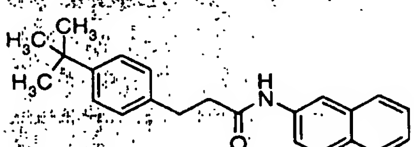


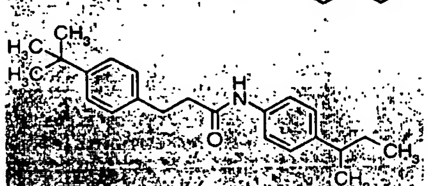


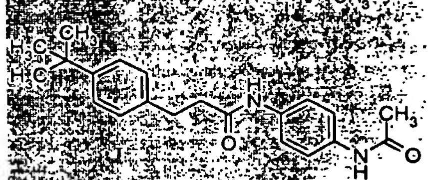


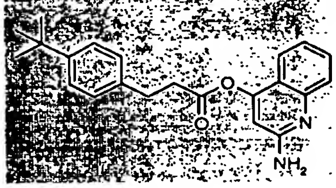


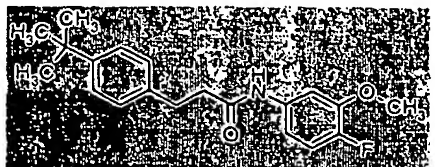


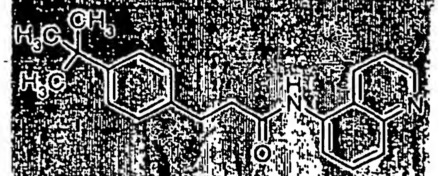


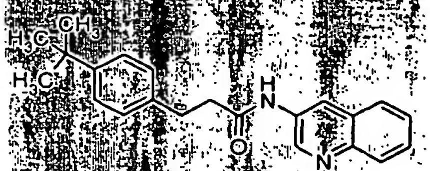


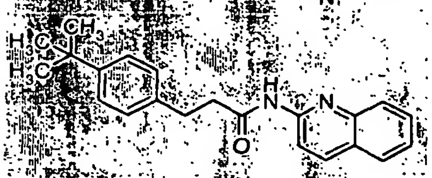


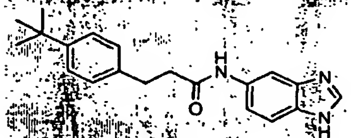


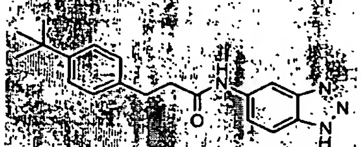


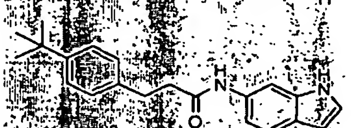


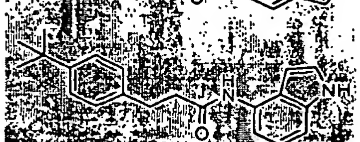


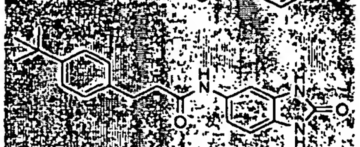


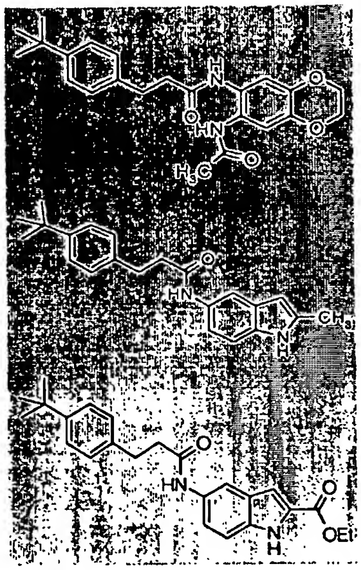


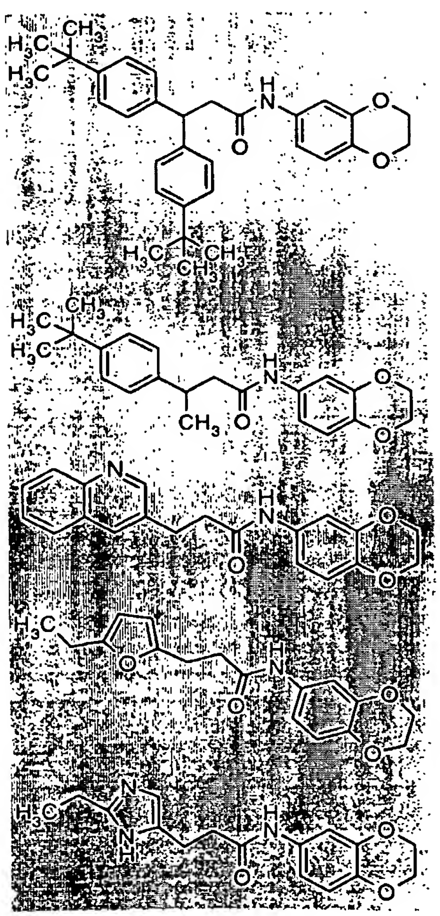


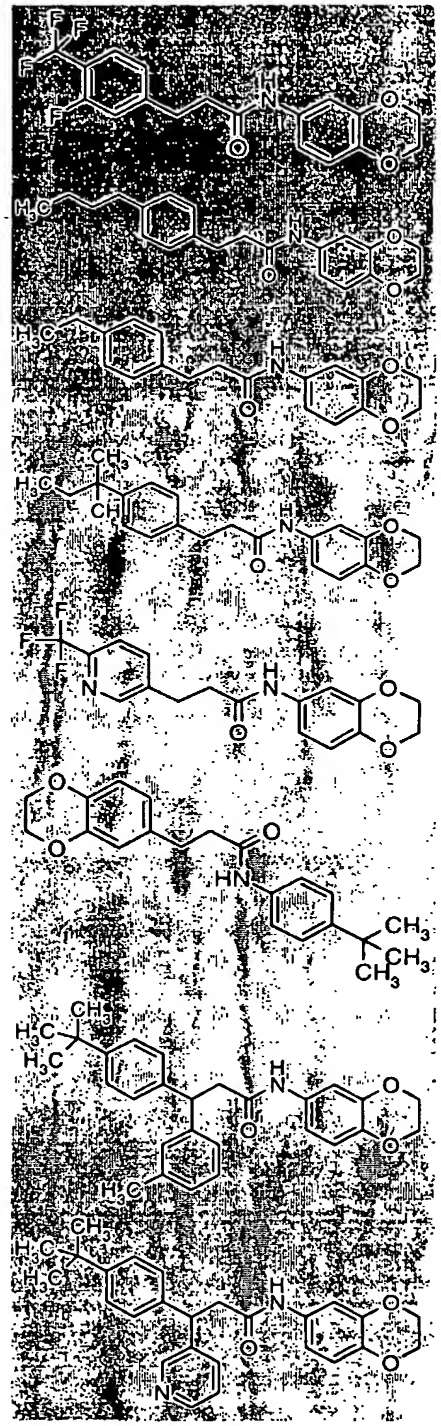


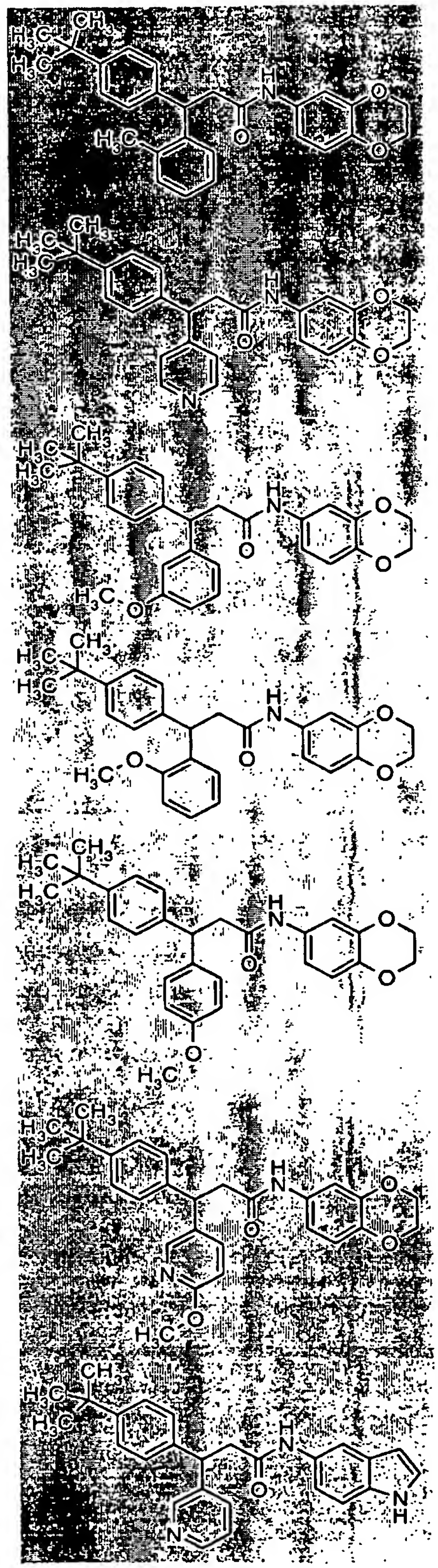


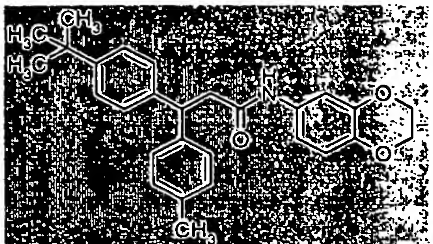


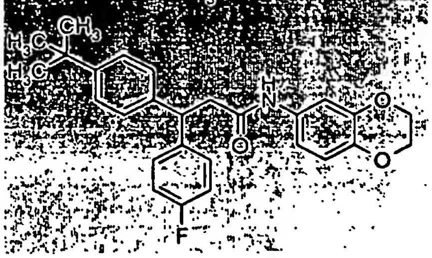


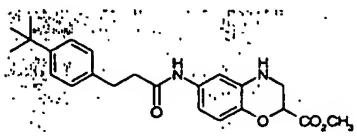


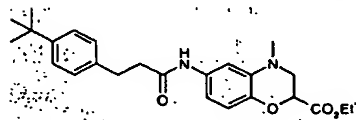


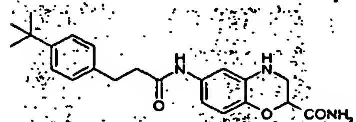


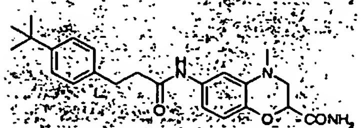


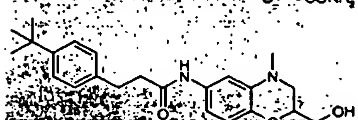


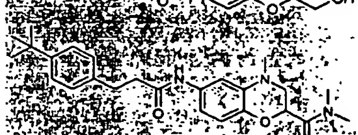


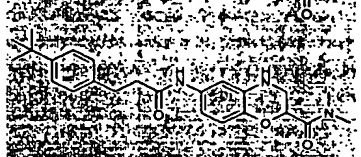


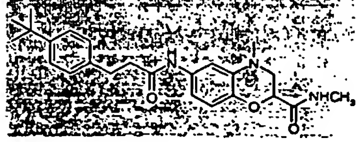


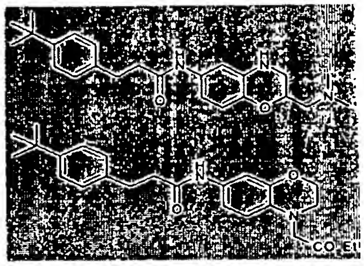


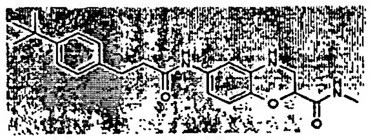


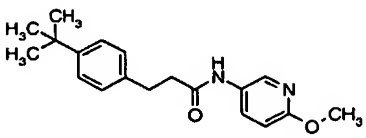


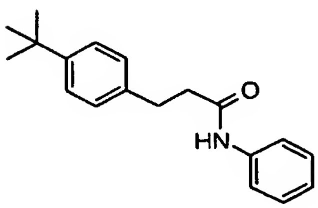


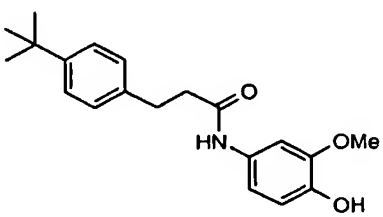


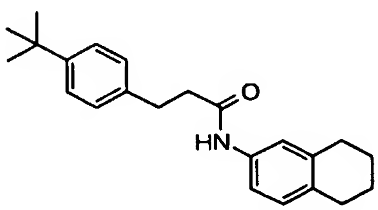


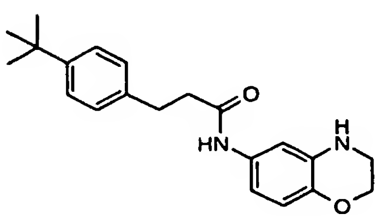


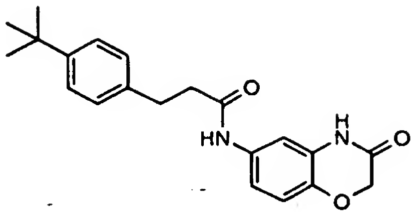


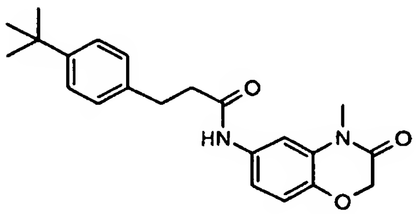


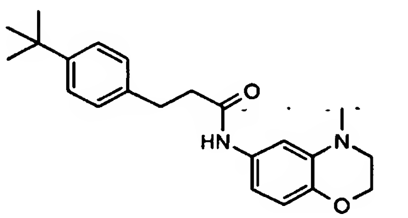


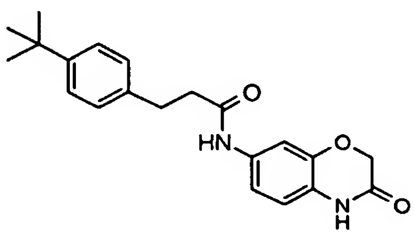


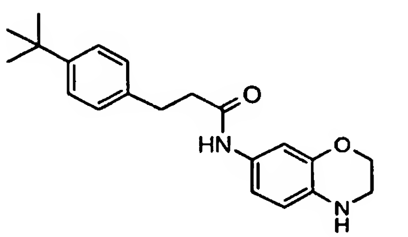


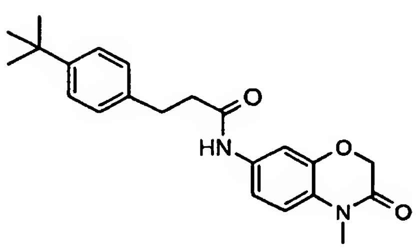


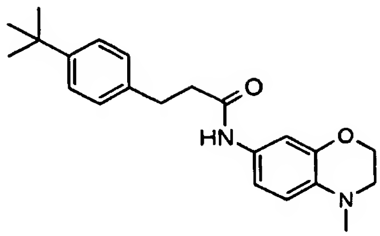


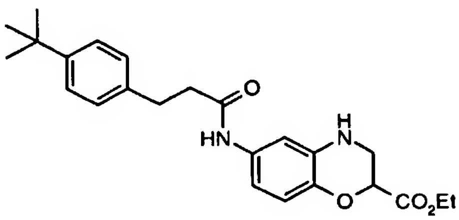


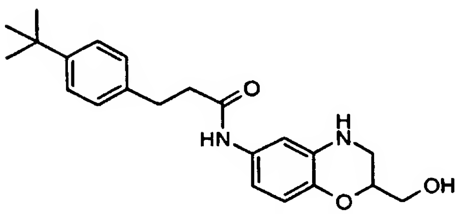


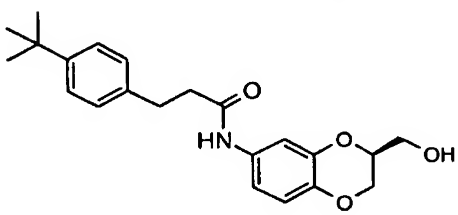


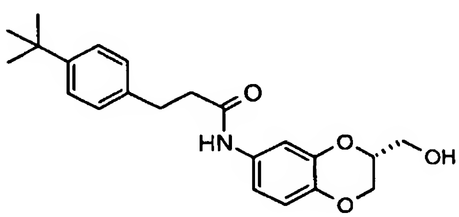


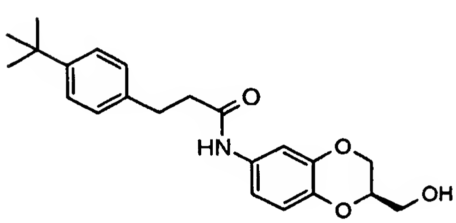


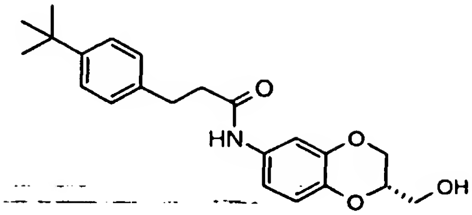


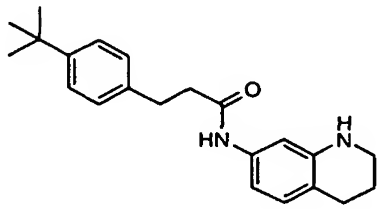


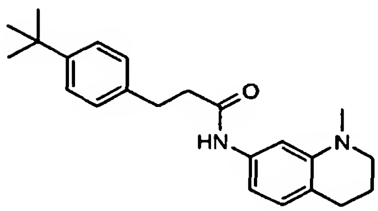


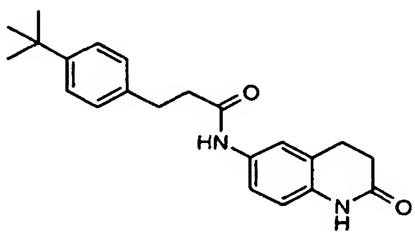


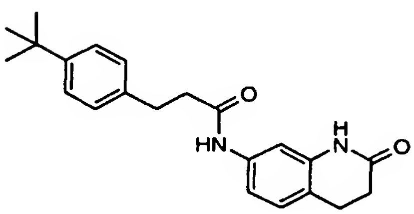


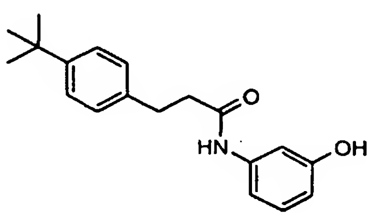


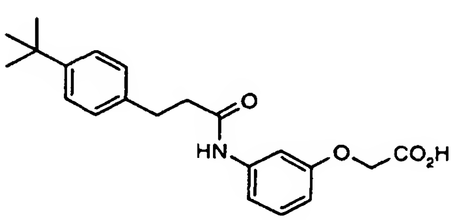


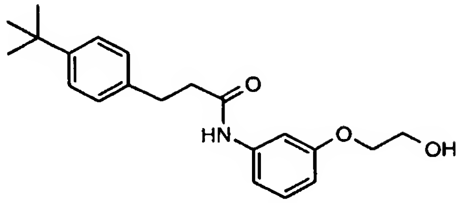


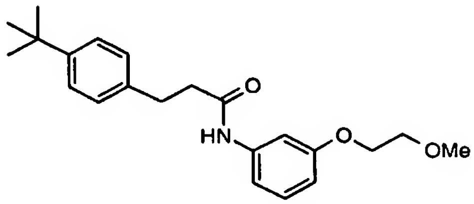


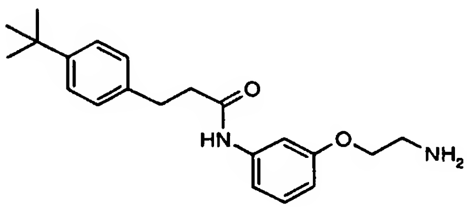


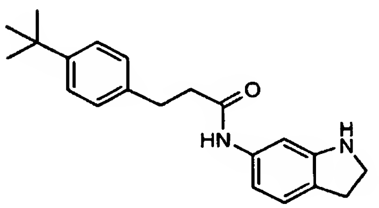


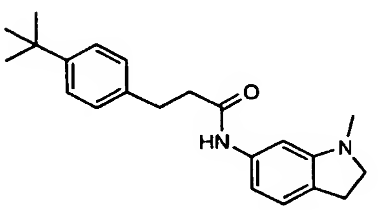


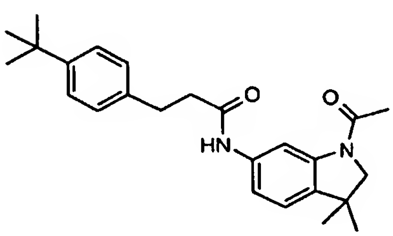


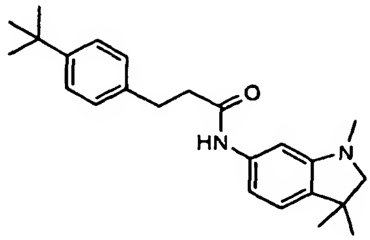


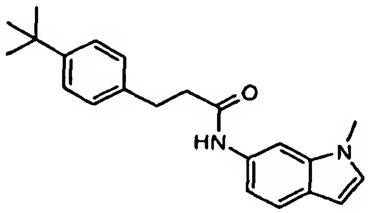


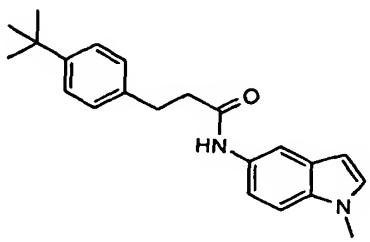


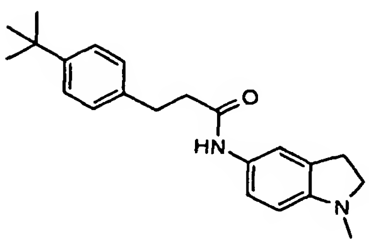


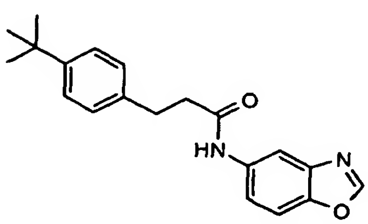


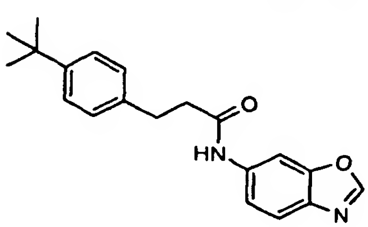


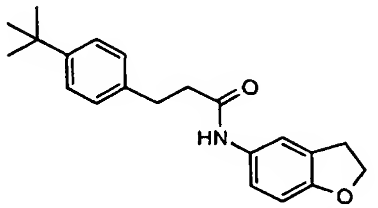


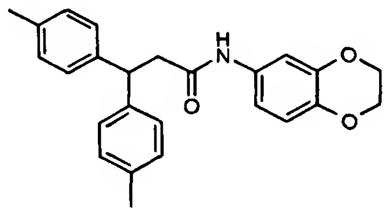


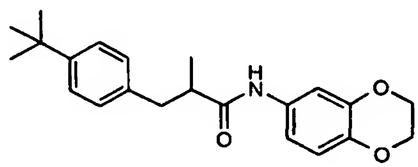


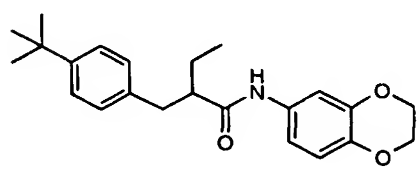


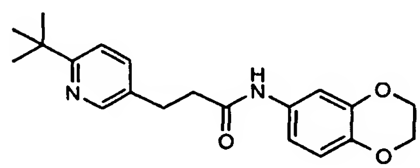


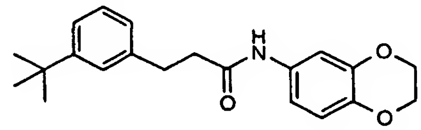


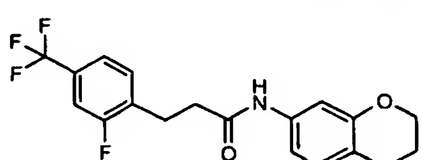


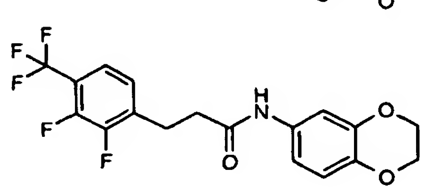


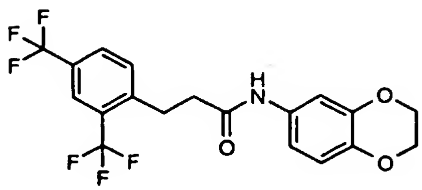


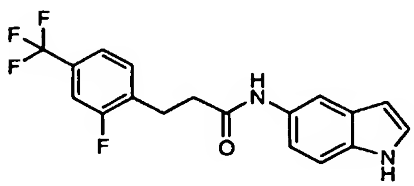


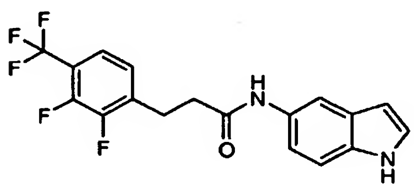


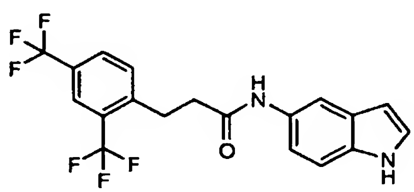


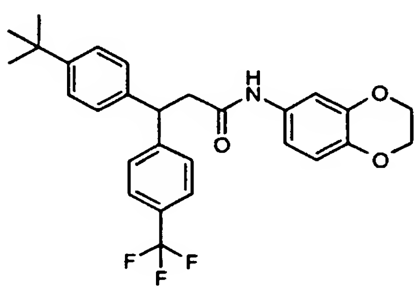


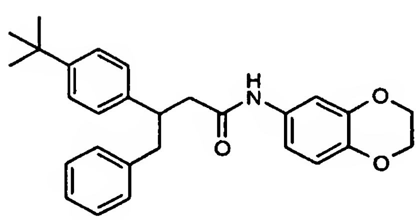


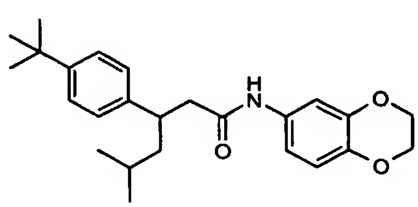


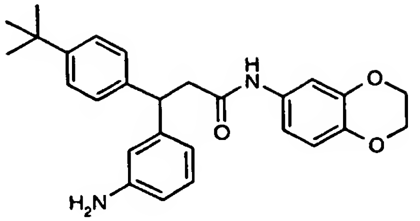








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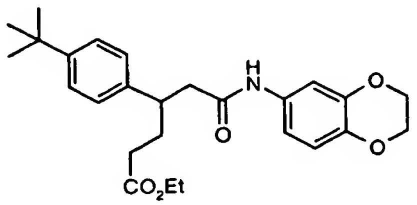
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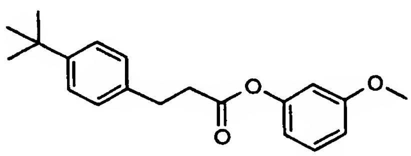
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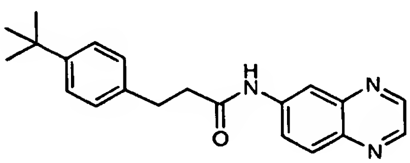
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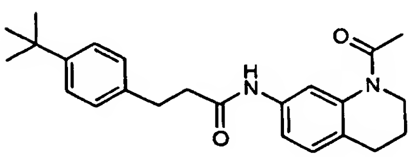
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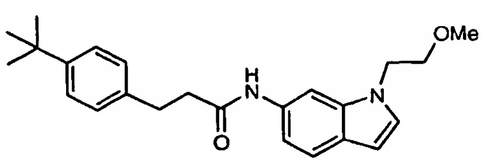
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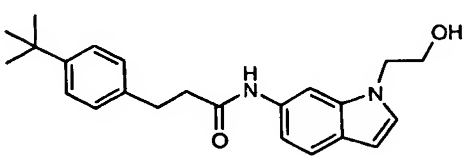
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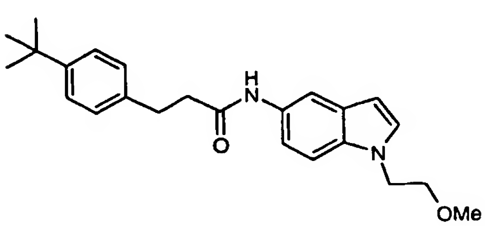
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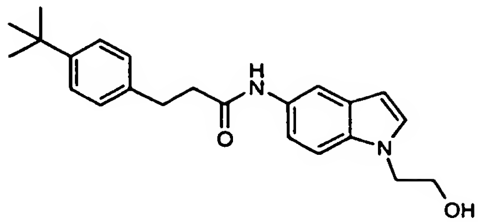
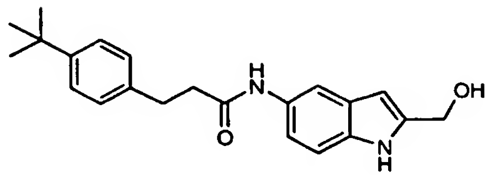
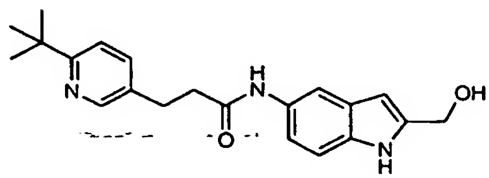
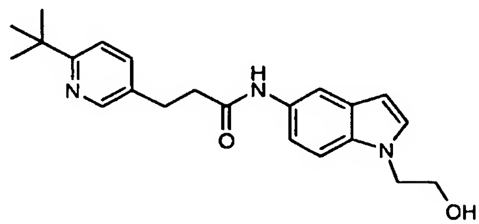
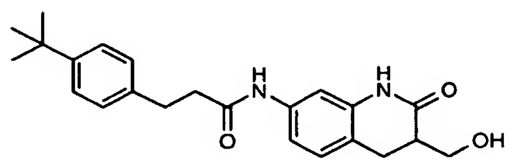
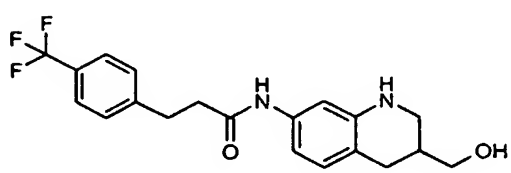


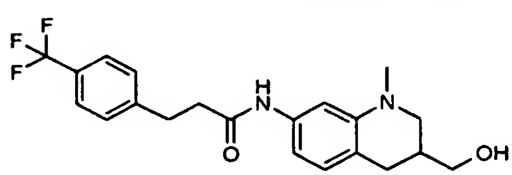


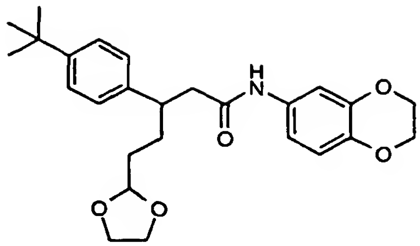


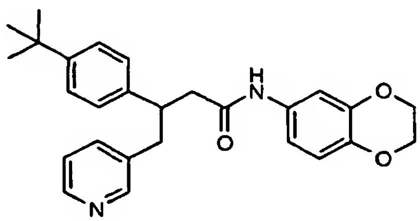


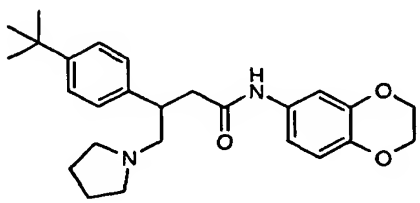


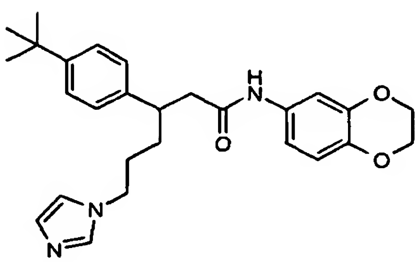


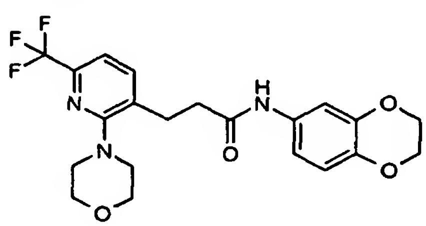


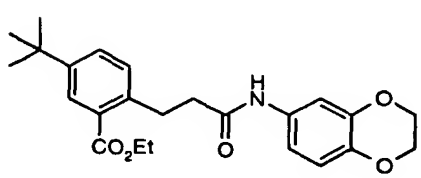


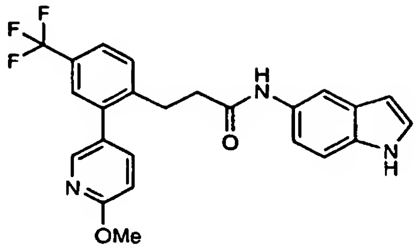


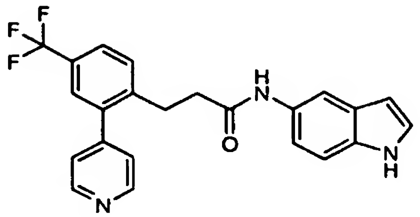


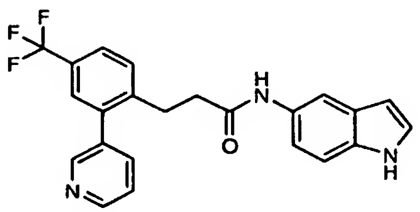


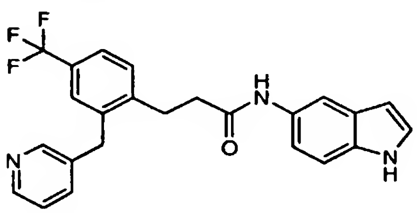


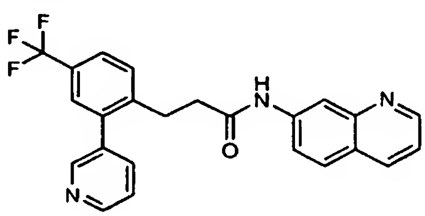


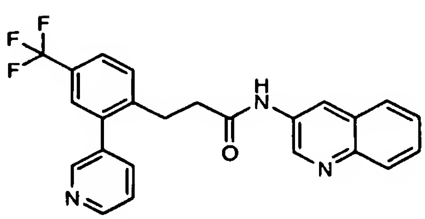


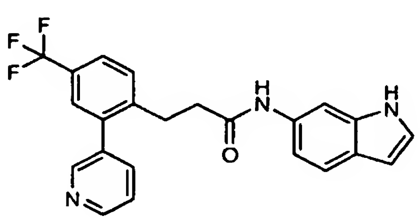


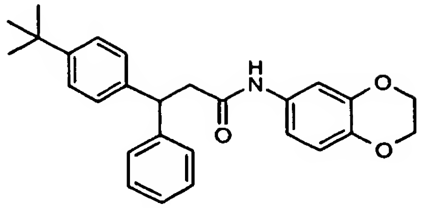


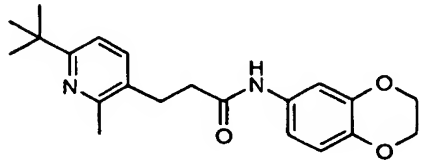


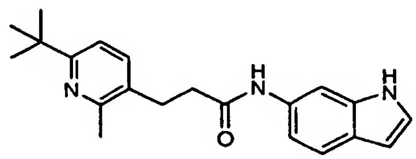


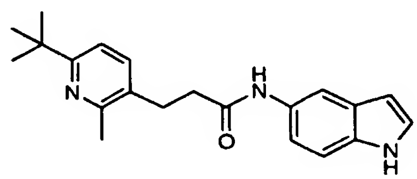


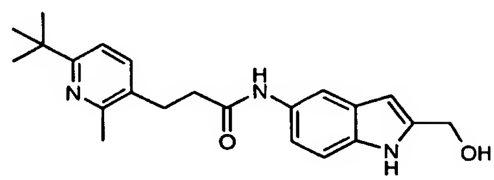


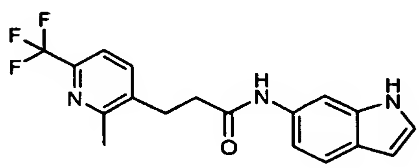


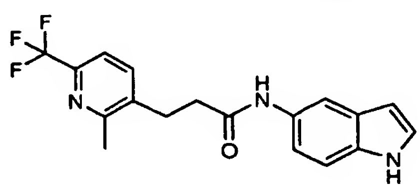


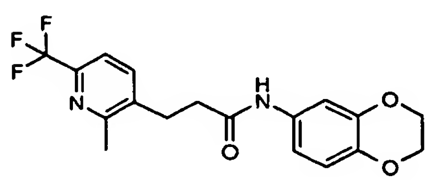


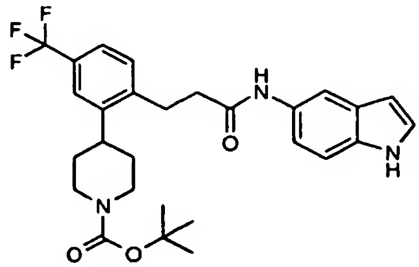


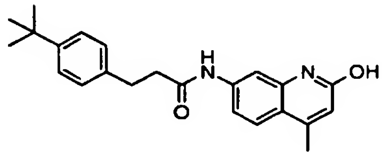


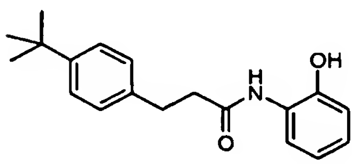


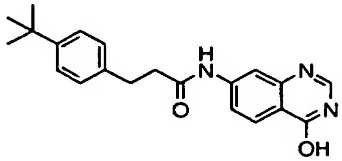


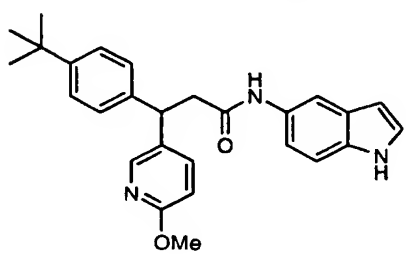


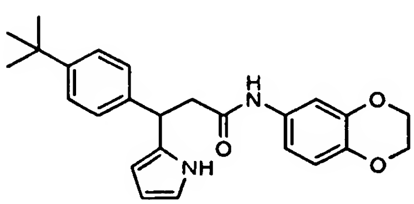


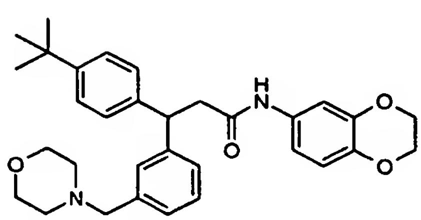


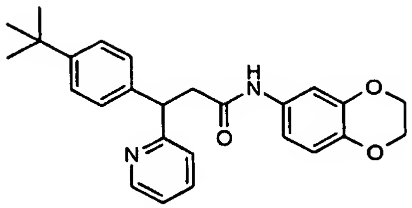


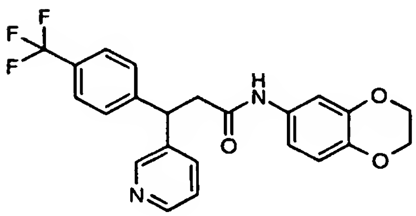


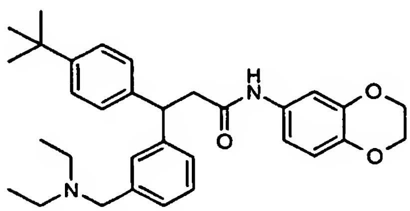


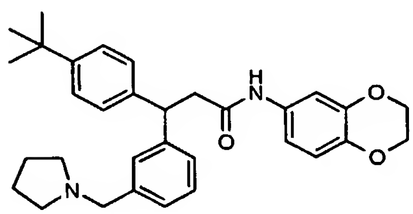


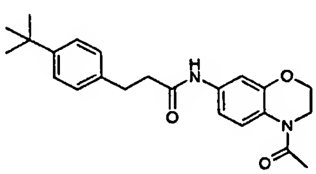


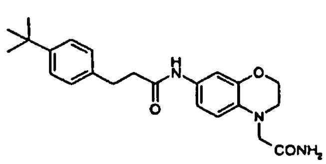


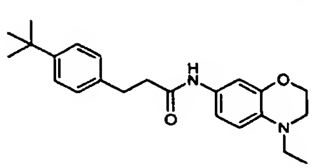


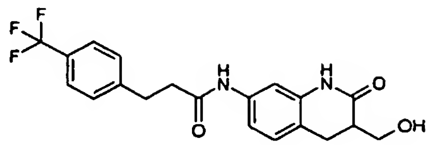


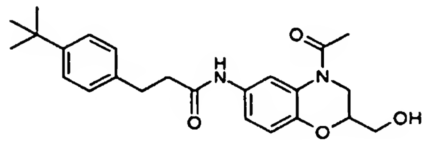


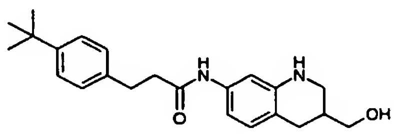


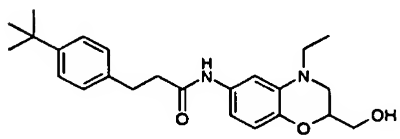


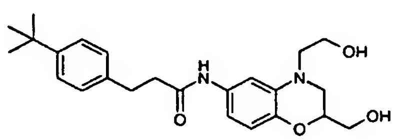


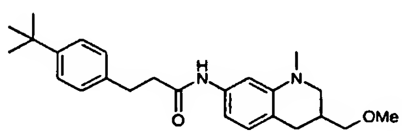


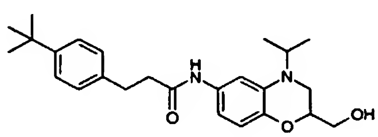


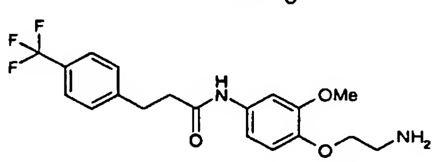


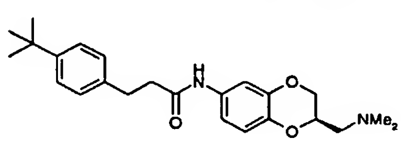


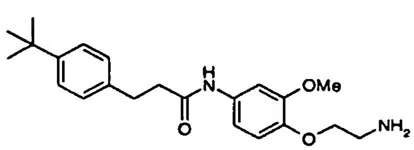


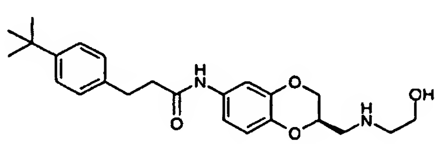


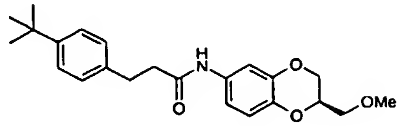


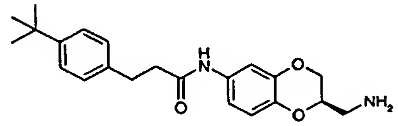


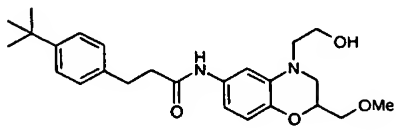


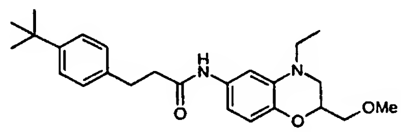


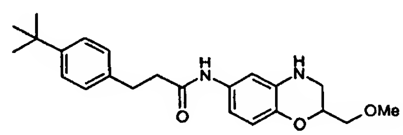


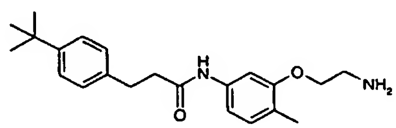


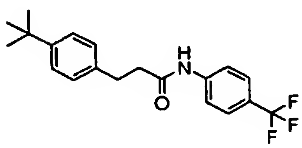


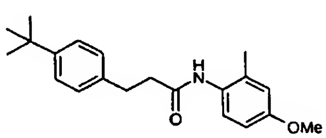


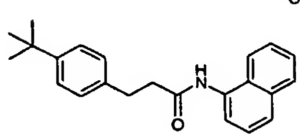


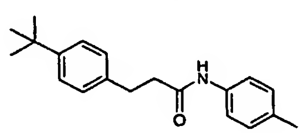


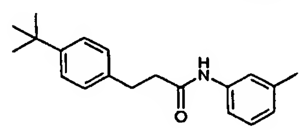


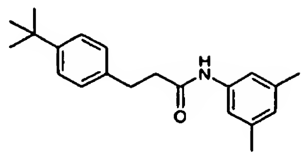


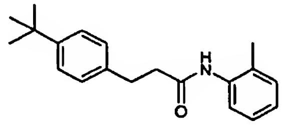


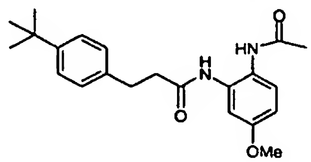


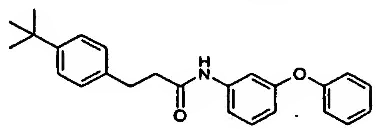


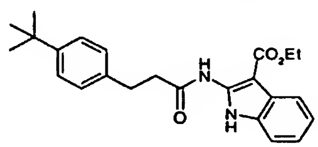


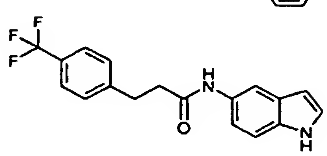


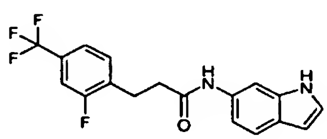


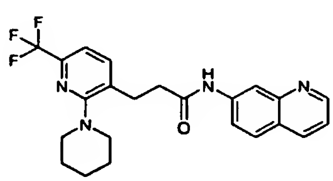


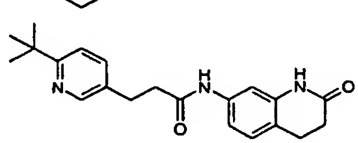


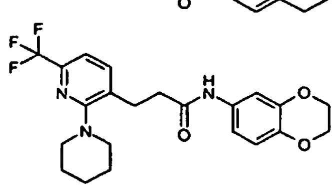


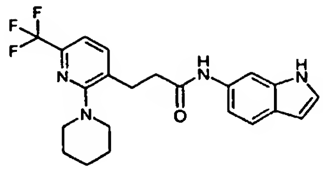


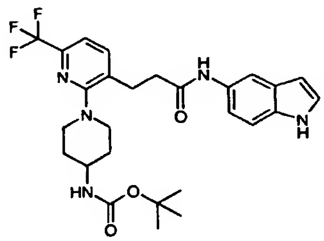


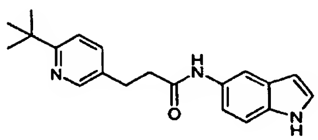


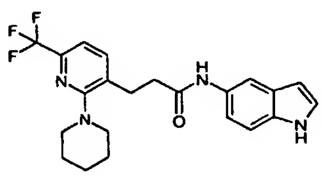


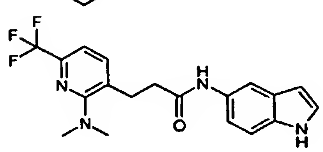


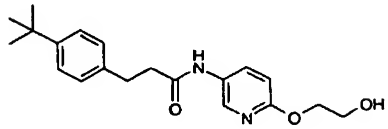


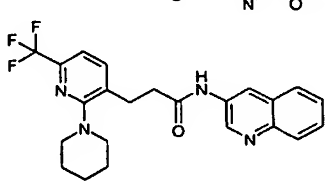


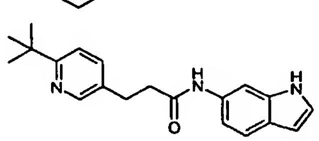


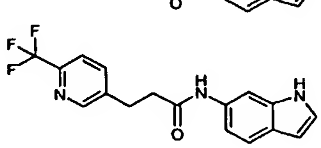


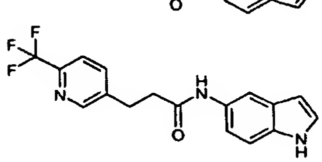


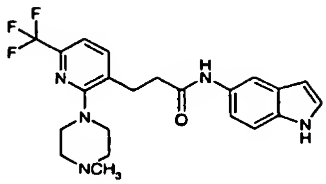


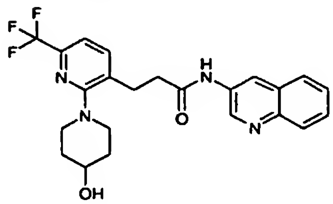


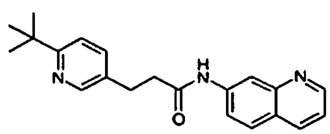


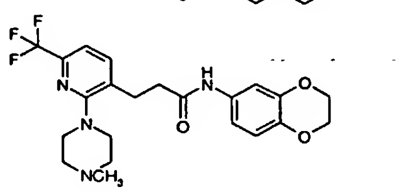


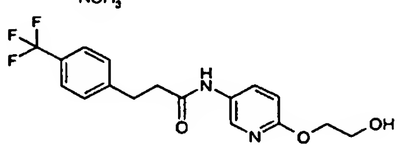


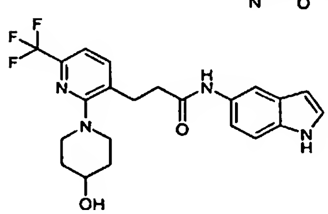


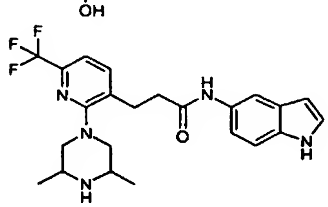


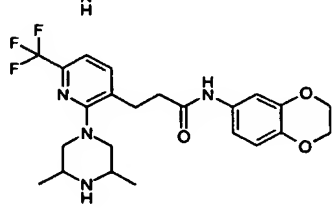


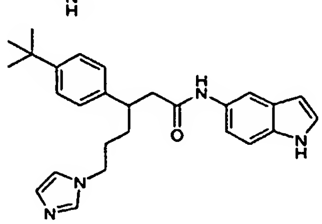


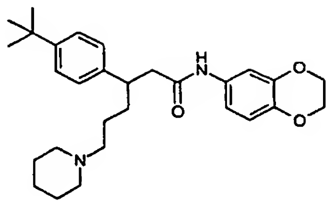


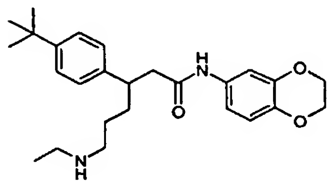


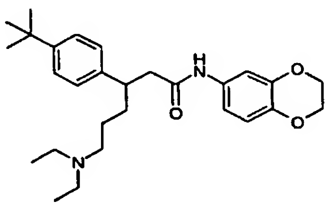


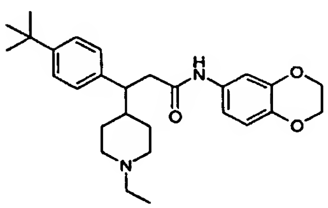


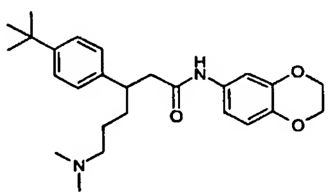


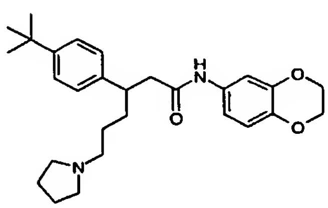


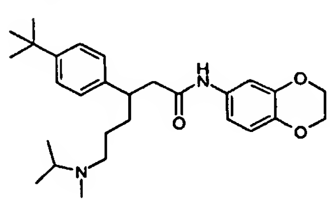


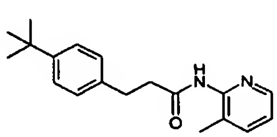


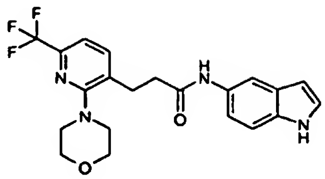


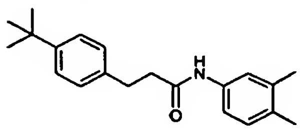


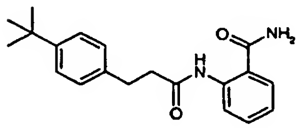


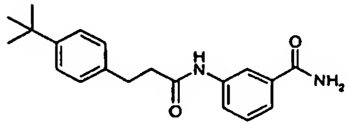


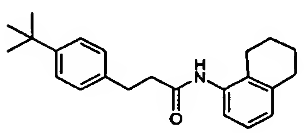


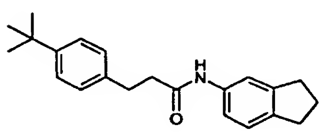


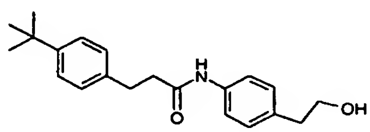


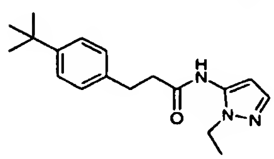


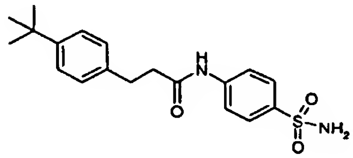


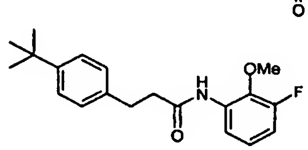


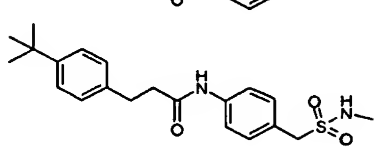


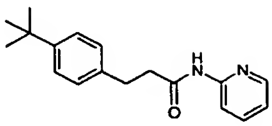


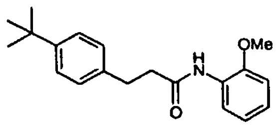


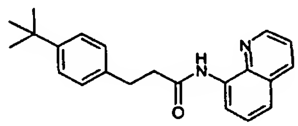


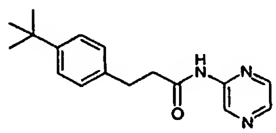


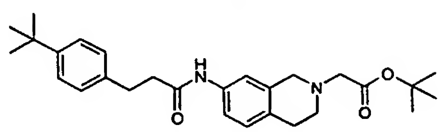


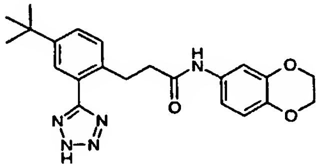


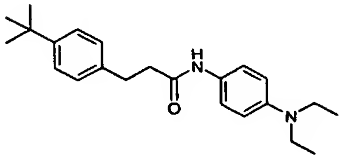


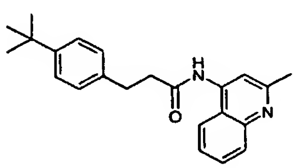


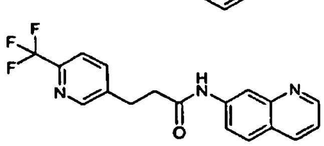


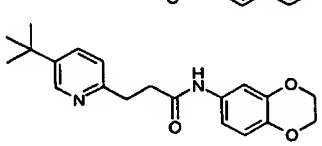




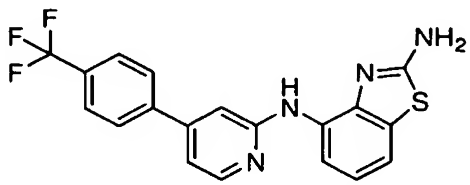


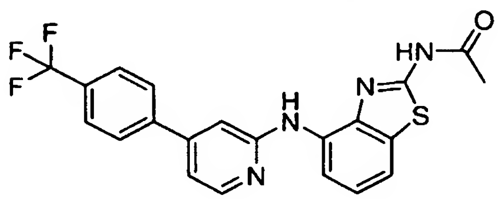


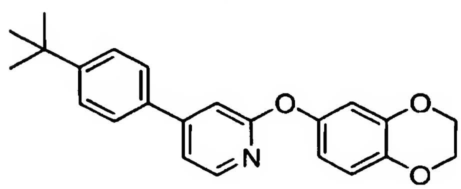


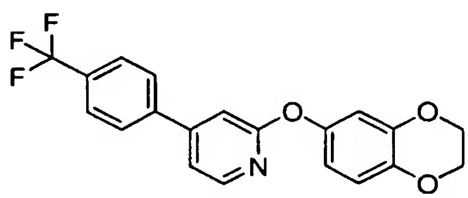


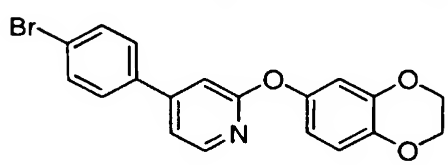
The following examples may also be made using the above generic schemes and synthetic examples:

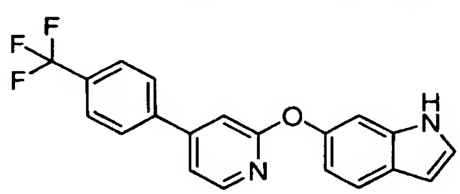


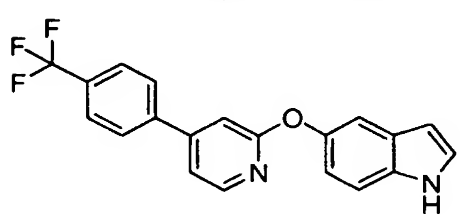


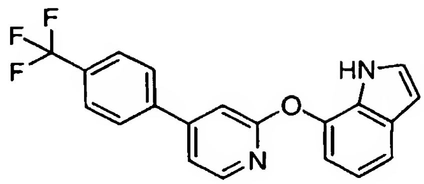


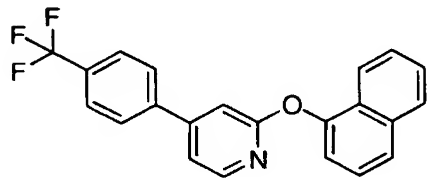


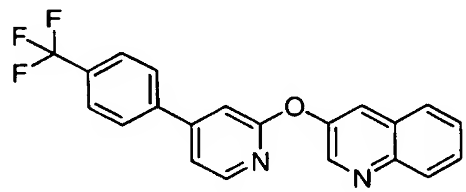


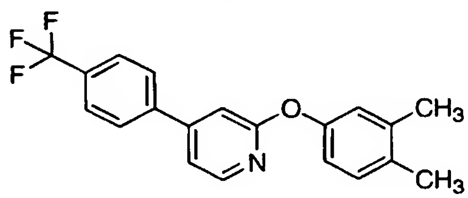


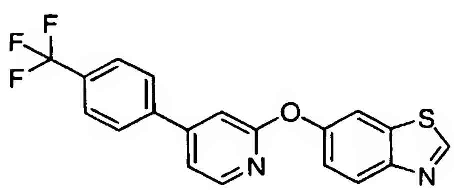


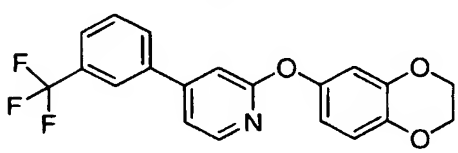


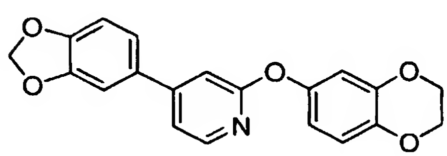


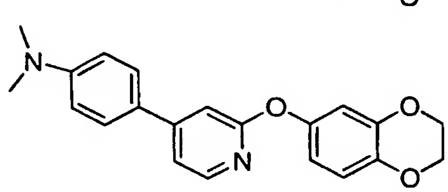


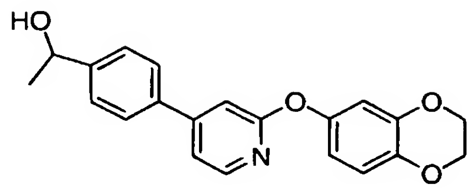












Capsaicin-induced Ca^{2+} influx in primary dorsal root ganglion neurons

Embryonic 19 day old (E19) dorsal root ganglia (DRG) were dissected from timed-pregnant, terminally anesthetized Sprague-Dawley rats (Charles River, Wilmington, MA) and collected in ice-cold L-15 media (Life Technologies, Grand Island, NY) containing 5% heat inactivated horse serum (Life Technologies). The DRG were then dissociated into single cell suspension using a papain dissociation system (Worthington Biochemical Corp., Freehold, NJ). The dissociated cells were pelleted at 200 x *g* for 5 min and re-suspended in EBSS containing 1 mg/ml ovomucoid inhibitor, 1 mg/ml ovalbumin and 0.005% DNase. Cell suspension was centrifuged through a gradient solution containing 10 mg/ml ovomucoid inhibitor, 10 mg/ml ovalbumin at 200 x *g* for 6 min to remove cell debris; and filtered through a 88-μm nylon mesh (Fisher Scientific, Pittsburgh, PA) to remove any clumps. Cell number was determined with a hemocytometer and cells were seeded into poly-ornithine 100 μg/ml (Sigma) and mouse laminin 1 μg/ml (Life Technologies)-coated 96-well plates at 10×10^3 cells/well in complete medium. The complete medium consists of minimal essential medium (MEM) and Ham's F12, 1:1, penicillin (100 U/ml), and streptomycin (100 μg/ml), and nerve growth factor (10ng/ml), 10% heat inactivated horse serum (Life Technologies). The cultures were kept at 37 °C, 5% CO_2 and 100% humidity. For controlling the growth of non-neuronal cells, 5-fluoro-2'-deoxyuridine (75μM) and uridine (180μM) were included in the medium. Activation of VR1 was achieved in these cellular assays using either a capsaicin stimulus (ranging from 0.01-10μM) or by an acid stimulus (addition of 30mM Hepes/Mes buffered at pH 4.1). Compounds were also tested in an assay format to evaluate their agonist properties at VR1. The activation of VR1 is followed as a function of cellular uptake of radioactive calcium ($^{45}Ca^{2+}$:Amersham CES3-2mCi).

Capsaicin Antagonist Assay: E-19 DRG cells at 3 days in culture are incubated with serial concentrations of VR1 antagonists, in HBSS (Hanks buffered saline solution supplemented with BSA 0.1mg/ml and 1 mM Hepes at pH 7.4) for 15 min, room temperature. Cells are then challenged with a VR1 agonist, capsaicin (500 nM), in activation buffer containing 0.1mg/ml BSA, 15 mM Hepes, pH 7.4, and 10 μCi/ml $^{45}Ca^{2+}$ (Amersham CES3-2mCi) in Ham's F12 for 2 min at room temperature.

Acid Antagonist Assay: Compounds are pre-incubated with E-19 DRG cells at room temperature for 2 minutes prior to addition of $^{45}Ca^{2+}$ in 30mM Hepes/Mes buffer (Final Assay pH 5) and then left for an additional 2 minutes prior to compound washout. Final concentration of $^{45}Ca^{2+}$ (Amersham CES3-2mCi) is 10 μCi/mL.

Agonist Assay: Compounds are incubated with E-19 DRG cells at room temperature for 2 minutes in the presence of $^{45}Ca^{2+}$ prior to compound washout. Final $^{45}Ca^{2+}$ (Amersham CES3-2mCi) at 10μCi/mL.

Compound Washout and Analysis: Assay plates are washed using an ELX405 plate washer (Bio-Tek Instruments Inc.) immediately after functional assay. Wash 3 X with PBS, 0.1 mg/mL BSA. Aspirate between washes. Read plates using a MicroBeta Jet (Wallac Inc.). Compound activity is then calculated using appropriate computational algorithms.

^{45}Calcium^{2+} Assay Protocol

Compounds may be assayed using Chinese Hamster Ovary cell lines stably expressing either human VR1 or rat VR1 under a CMV promoter. Cells could be cultured in a Growth Medium, routinely passaged at 70% confluency using trypsin and plated in an assay plate 24 hours prior to compound evaluation.

Possible Growth Medium:

DMEM, high glucose (Gibco 11965-084).

10% Dialyzed serum (Hyclone SH30079.03).

1X Non-Essential Amino Acids (Gibco 11140-050).

1X Glutamine-Pen-Strep (Gibco 10378-016).

Geneticin, 450μg/mL (Gibco 10131-035).

Compounds could be diluted in 100% DMSO and tested for activity over several log units of concentration [40µM-2pM]. Compounds may be further diluted in HBSS buffer (pH 7.4) 0.1 mg/mL BSA, prior to evaluation. Final DMSO concentration in assay would be 0.5-1%. Each assay plate could be controlled with a buffer only and a known antagonist compound (either capsazepine or one of the described VR1 antagonists).

Activation of VR1 could be achieved in these cellular assays using either a capsaicin stimulus (ranging from 0.1-1µM) or by an acid stimulus (addition of 30mM Hepes/Mes buffered at pH 4.1). Compounds could also be tested in an assay format to evaluate their agonist properties at VR1.

Capsaicin Antagonist Assay: Compounds may be pre-incubated with cells (expressing either human or rat VR1) at room temperature for 2 minutes prior to addition of $^{45}Ca^{2+}$ and Capsaicin and then left for an additional 2 minutes prior to compound washout. Capsaicin (200nM) can be added in HAM's F12, 0.1 mg/mL BSA, 15 mM Hepes at pH 7.4. Final $^{45}Ca^{2+}$ (Amersham CES3-2mCi) added could be 10µCi/mL.

Acid Antagonist Assay: Compounds can be pre-incubated with cells (expressing either human or rat VR1) for 2 minutes prior to addition of $^{45}Ca^{2+}$ in 30mM Hepes/Mes buffer (Final Assay pH 5) and then left for an additional 2 minutes prior to compound washout. Final $^{45}Ca^{2+}$ (Amersham CES3-2mCi) added could be 10µCi/mL.

Agonist Assay: Compounds can be incubated with cells (expressing either human or rat VR1) for 2 minutes in the presence of $^{45}Ca^{2+}$ prior to compound washout. Final $^{45}Ca^{2+}$ (Amersham CES3-2mCi) added could be 10µCi/mL.

Compound Washout and Analysis: Assay plates would be washed using an ELX405 plate washer (Bio-Tek Instruments Inc.) immediately after the functional assay. One could wash 3 X with PBS, 0.1 mg/mL BSA, aspirating between washes. Plates could then be read using a MicroBeta Jet (Wallac Inc.) and compound activity calculated using appropriate computational algorithms.

Useful nucleic acid sequences and proteins may be found in U.S. Patent Nos. 6,335,180, 6, 406,908 and 6,239,267, herein incorporated by reference in their entirety.

For the treatment of vanilloid-receptor-diseases, such as acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, the compounds of the present invention may be administered orally, parentally, by inhalation spray, rectally, or topically in dosage unit formulations containing conventional pharmaceutically acceptable carriers, adjuvants, and vehicles. The term parenteral as used herein includes, subcutaneous, intravenous, intramuscular, intrasternal, infusion techniques or intraperitoneally.

Treatment of diseases and disorders herein is intended to also include the prophylactic administration of a compound of the invention, a pharmaceutical salt thereof, or a pharmaceutical composition of either to a subject (*i.e.*, an animal, preferably a mammal, most preferably a human) believed to be in need of preventative treatment, such as, for example, pain, inflammation and the like.

The dosage regimen for treating vanilloid-receptor-mediated diseases, cancer, and/or hyperglycemia with the compounds of this invention and/or compositions of this invention is based on a variety of factors, including the type of disease, the age, weight, sex, medical condition of the patient, the severity of the condition, the route of administration, and the particular compound employed. Thus, the dosage regimen may vary widely, but can be determined routinely using standard methods. Dosage levels of the order from about 0.01 mg to 30 mg per

kilogram of body weight per day, preferably from about 0.1 mg to 10 mg/kg, more preferably from about 0.25 mg to 1 mg/kg are useful for all methods of use disclosed herein.

The pharmaceutically active compounds of this invention can be processed in accordance with conventional methods of pharmacy to produce medicinal agents for administration to patients, including humans and other mammals.

For oral administration, the pharmaceutical composition may be in the form of, for example, a capsule, a tablet, a suspension, or liquid. The pharmaceutical composition is preferably made in the form of a dosage unit containing a given amount of the active ingredient. For example, these may contain an amount of active ingredient from about 1 to 2000 mg, preferably from about 1 to 500 mg, more preferably from about 5 to 150 mg. A suitable daily dose for a human or other mammal may vary widely depending on the condition of the patient and other factors, but, once again, can be determined using routine methods.

The active ingredient may also be administered by injection as a composition with suitable carriers including saline, dextrose, or water. The daily parenteral dosage regimen will be from about 0.1 to about 30 mg/kg of total body weight, preferably from about 0.1 to about 10 mg/kg, and more preferably from about 0.25 mg to 1 mg/kg.

Injectable preparations, such as sterile injectable aqueous or oleaginous suspensions, may be formulated according to the known are using suitable dispersing or wetting agents and suspending agents. The sterile injectable preparation may also be a sterile injectable solution or suspension in a non-toxic parenterally acceptable diluent or solvent, for example as a solution in 1,3-butanediol. Among the acceptable vehicles and solvents that may be employed are water, Ringer's solution, and isotonic sodium chloride solution. In addition, sterile, fixed oils are conventionally employed as a solvent or suspending medium. For this purpose any bland fixed oil may be employed, including synthetic mono- or diglycerides. In addition, fatty acids such as oleic acid find use in the preparation of injectables.

Suppositories for rectal administration of the drug can be prepared by mixing the drug with a suitable non-irritating excipient such as cocoa butter and polyethylene glycols that are solid at ordinary temperatures but liquid at the rectal temperature and will therefore melt in the rectum and release the drug.

A suitable topical dose of active ingredient of a compound of the invention is 0.1 mg to 150 mg administered one to four, preferably one or two times daily. For topical administration, the active ingredient may comprise from 0.001% to 10% w/w, *e.g.*, from 1% to 2% by weight of the formulation, although it may comprise as much as 10% w/w, but preferably not more than 5% w/w, and more preferably from 0.1% to 1% of the formulation.

Formulations suitable for topical administration include liquid or semi-liquid preparations suitable for penetration through the skin (*e.g.*, liniments, lotions, ointments, creams, or pastes) and drops suitable for administration to the eye, ear, or nose.

For administration, the compounds of this invention are ordinarily combined with one or more adjuvants appropriate for the indicated route of administration. The compounds may be admixed with lactose, sucrose, starch powder, cellulose esters of alkanoic acids, stearic acid, talc, magnesium stearate, magnesium oxide, sodium and calcium salts of phosphoric and sulfuric acids, acacia, gelatin, sodium alginate, polyvinyl-pyrrolidine, and/or polyvinyl alcohol, and tableted or encapsulated for conventional administration. Alternatively, the compounds of this invention may be dissolved in saline, water, polyethylene glycol, propylene glycol, ethanol, corn oil, peanut oil, cottonseed oil, sesame oil, tragacanth gum, and/or various buffers. Other adjuvants and modes of administration are well known in the pharmaceutical art. The carrier or diluent may include time delay material, such as glyceryl monostearate or glyceryl distearate alone or with a wax, or other materials well known in the art.

The pharmaceutical compositions may be made up in a solid form (including granules, powders or suppositories) or in a liquid form (*e.g.*, solutions, suspensions, or emulsions). The pharmaceutical compositions may be subjected to conventional pharmaceutical operations such as sterilization and/or may contain

conventional adjuvants, such as preservatives, stabilizers, wetting agents, emulsifiers, buffers etc.

Solid dosage forms for oral administration may include capsules, tablets, pills, powders, and granules. In such solid dosage forms, the active compound may be admixed with at least one inert diluent such as sucrose, lactose, or starch. Such dosage forms may also comprise, as in normal practice, additional substances other than inert diluents, *e.g.*, lubricating agents such as magnesium stearate. In the case of capsules, tablets, and pills, the dosage forms may also comprise buffering agents. Tablets and pills can additionally be prepared with enteric coatings.

Liquid dosage forms for oral administration may include pharmaceutically acceptable emulsions, solutions, suspensions, syrups, and elixirs containing inert diluents commonly used in the art, such as water. Such compositions may also comprise adjuvants, such as wetting, sweetening, flavoring, and perfuming agents.

Compounds of the present invention can possess one or more asymmetric carbon atoms and are thus capable of existing in the form of optical isomers as well as in the form of racemic or non-racemic mixtures thereof. The optical isomers can be obtained by resolution of the racemic mixtures according to conventional processes, *e.g.*, by formation of diastereoisomeric salts, by treatment with an optically active acid or base. Examples of appropriate acids are tartaric, diacetyltartaric, dibenzoyltartaric, ditoluoyltartaric, and camphorsulfonic acid and then separation of the mixture of diastereoisomers by crystallization followed by liberation of the optically active bases from these salts. A different process for separation of optical isomers involves the use of a chiral chromatography column optimally chosen to maximize the separation of the enantiomers. Still another available method involves synthesis of covalent diastereoisomeric molecules by reacting compounds of the invention with an optically pure acid in an activated form or an optically pure isocyanate. The synthesized diastereoisomers can be separated by conventional means such as chromatography, distillation, crystallization or sublimation, and then hydrolyzed to deliver the enantiomerically pure compound. The optically active compounds of the invention can likewise be

obtained by using active starting materials. These isomers may be in the form of a free acid, a free base, an ester or a salt.

Likewise, the compounds of this invention may exist as isomers, that is compounds of the same molecular formula but in which the atoms, relative to one another, are arranged differently. In particular, the alkylene substituents of the compounds of this invention, are normally and preferably arranged and inserted into the molecules as indicated in the definitions for each of these groups, being read from left to right. However, in certain cases, one skilled in the art will appreciate that it is possible to prepare compounds of this invention in which these substituents are reversed in orientation relative to the other atoms in the molecule. That is, the substituent to be inserted may be the same as that noted above except that it is inserted into the molecule in the reverse orientation. One skilled in the art will appreciate that these isomeric forms of the compounds of this invention are to be construed as encompassed within the scope of the present invention.

The compounds of the present invention can be used in the form of salts derived from inorganic or organic acids. The salts include, but are not limited to, the following: acetate, adipate, alginate, citrate, aspartate, benzoate, benzenesulfonate, bisulfate, butyrate, camphorate, camphorsulfonate, digluconate, cyclopentanepropionate, dodecylsulfate, ethanesulfonate, glucoheptanoate, glycerophosphate, hemisulfate, heptanoate, hexanoate, fumarate, hydrochloride, hydrobromide, hydroiodide, 2-hydroxyethanesulfonate, lactate, maleate, methansulfonate, nicotinate, 2-naphthalenesulfonate, oxalate, palmoate, pectinate, persulfate, 2-phenylpropionate, picrate, pivalate, propionate, succinate, tartrate, thiocyanate, tosylate, mesylate, and undecanoate. Also, the basic nitrogen-containing groups can be quaternized with such agents as lower alkyl halides, such as methyl, ethyl, propyl, and butyl chloride, bromides and iodides; dialkyl sulfates like dimethyl, diethyl, dibutyl, and diamyl sulfates, long chain halides such as decyl, lauryl, myristyl and stearyl chlorides, bromides and iodides, aralkyl halides like benzyl and phenethyl bromides, and others. Water or oil-soluble or dispersible products are thereby obtained.

Examples of acids that may be employed to from pharmaceutically acceptable acid addition salts include such inorganic acids as hydrochloric acid,

sulfuric acid and phosphoric acid and such organic acids as oxalic acid, maleic acid, succinic acid and citric acid. Other examples include salts with alkali metals or alkaline earth metals, such as sodium, potassium, calcium or magnesium or with organic bases.

Also encompassed in the scope of the present invention are pharmaceutically acceptable esters of a carboxylic acid or hydroxyl containing group, including a metabolically labile ester or a prodrug form of a compound of this invention. A metabolically labile ester is one which may produce, for example, an increase in blood levels and prolong the efficacy of the corresponding non-esterified form of the compound. A prodrug form is one that is not in an active form of the molecule as administered but which becomes therapeutically active after some in vivo activity or biotransformation, such as metabolism, for example, enzymatic or hydrolytic cleavage. For a general discussion of prodrugs involving esters see Svensson and Tunek Drug Metabolism Reviews 165 (1988) and Bundgaard Design of Prodrugs, Elsevier (1985). Examples of a masked carboxylate anion include a variety of esters, such as alkyl (for example, methyl, ethyl), cycloalkyl (for example, cyclohexyl), aralkyl (for example, benzyl, p-methoxybenzyl), and alkylcarbonyloxyalkyl (for example, pivaloyloxymethyl). Amines have been masked as arylcarbonyloxymethyl substituted derivatives which are cleaved by esterases in vivo releasing the free drug and formaldehyde (Bungaard J. Med. Chem. 2503 (1989)). Also, drugs containing an acidic NH group, such as imidazole, imide, indole and the like, have been masked with N-acyloxymethyl groups (Bundgaard Design of Prodrugs, Elsevier (1985)). Hydroxy groups have been masked as esters and ethers. EP 039,051 (Sloan and Little, 4/11/81) discloses Mannich-base hydroxamic acid prodrugs, their preparation and use. Esters of a compound of this invention, may include, for example, the methyl, ethyl, propyl, and butyl esters, as well as other suitable esters formed between an acidic moiety and a hydroxyl containing moiety. Metabolically labile esters, may include, for example, methoxymethyl, ethoxymethyl, iso-propoxymethyl, α-methoxyethyl, groups such as α-((C_1-C_4)alkyloxy)ethyl, for example, methoxyethyl, ethoxyethyl, propoxyethyl, iso-propoxyethyl, etc.; 2-oxo-1,3-dioxolen-4-ylmethyl groups, such as 5-methyl-

2-oxo-1,3,dioxolen-4-ylmethyl, etc.; C_1-C_3 alkylthiomethyl groups, for example, methylthiomethyl, ethylthiomethyl, isopropylthiomethyl, etc.; acyloxymethyl groups, for example, pivaloyloxymethyl, α-acetoxymethyl, etc.; ethoxycarbonyl-1-methyl; or α-acyloxy-α-substituted methyl groups, for example α-acetoxyethyl.

Further, the compounds of the invention may exist as crystalline solids which can be crystallized from common solvents such as ethanol, N,N-dimethyl-formamide, water, or the like. Thus, crystalline forms of the compounds of the invention may exist as polymorphs, solvates and/or hydrates of the parent compounds or their pharmaceutically acceptable salts. All of such forms likewise are to be construed as falling within the scope of the invention.

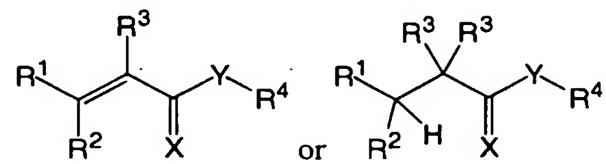
While the compounds of the invention can be administered as the sole active pharmaceutical agent, they can also be used in combination with one or more compounds of the invention or other agents. When administered as a combination, the therapeutic agents can be formulated as separate compositions that are given at the same time or different times, or the therapeutic agents can be given as a single composition.

The foregoing is merely illustrative of the invention and is not intended to limit the invention to the disclosed compounds. Variations and changes, which are obvious to one skilled in the art are intended to be within the scope and nature of the invention which are defined in the appended claims.

From the foregoing description, one skilled in the art can easily ascertain the essential characteristics of this invention, and without departing from the spirit and scope thereof, can make various changes and modifications of the invention to adapt it to various usages and conditions.

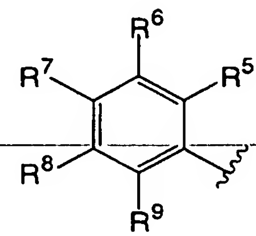
We Claim:

1. A compound having the structure:



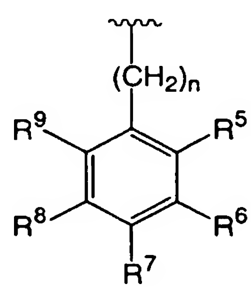
wherein:

R^1 is



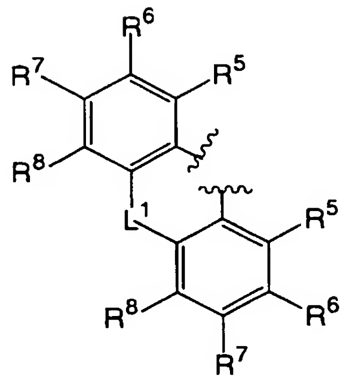
or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},



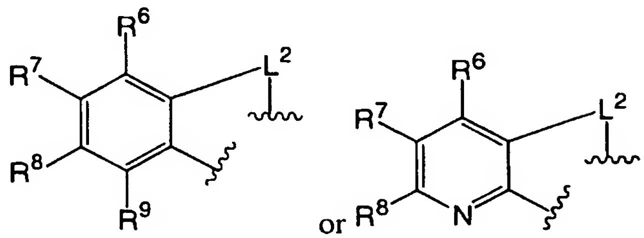
or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

or R^1 and R^2 together are

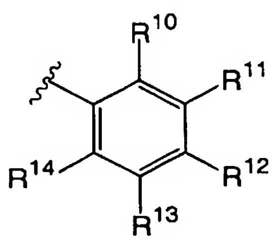


;

R^3 is H or C_{1-4}alkyl; or R^1 and R^3 together are



R^4 is



; or

R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^aR^a, $-O-C_{1-6}$alkylOR^a, $-O-C_{1-6}$alkyl$C(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}$haloalkyl, $-NR^a-C_{1-6}$alkylNR^aR^a, $-NR^a-C_{1-6}$alkylOR^a, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^aC_{1-6}$alkyl and $-NR^aC(=O)C_{1-6}$alkyl; or R^4 is 10-membered bicyclic ring

comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O; except that when R^1 is 4-chlorophenyl, 3-bromophenyl, 3-nitrophenyl, 2-nitro-3-chlorophenyl, 3,4-methylenedioxyphenyl, 3-methylthiophenyl or 2,3,4-methoxyphenyl, then R^4 is not phenyl substituted by 1 or 2 substituents selected from halo and C_{1-4}alkyl; and R^1 and R^4 are not both 3,4-methylenedioxyphenyl; and when R^1 is 4-trifluoromethylphenyl, then R^4 is not pyridinyl, 2-methyl-4-aminoquinolinyl or 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl;

R^5 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S;

R^6 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a; or R^5 and R^6 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-6}alkyl, (=O), -OC_{1-6}alkyl, -NR^aC_{1-6}alkyl, -C_{1-6}alkylOR^a and C_{1-6}alkylNR^aR^a, and the available N atoms of the bridge are substituted by R^a, -C_{1-6}alkylOR^a or C_{1-6}alkylNR^aR^a;

R^7 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a;

R^8 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a; or R^7

and R^8 together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the bridge are substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-6}alkyl, (=O), -O-C_{1-6}alkyl, -NR^aC_{1-6}alkyl, -C_{1-6}alkylOR^a and C_{1-6}alkylNR^aR^a, and the available N atoms of the bridge are substituted by R^a, -C_{1-6}alkylOR^a or C_{1-6}alkylNR^aR^a;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a or -NR^a-C_{1-6}alkylOR^a;

R^{10} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)$OC_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^aC_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl;

R^{11} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$$C_{1-6}$alkyl, -O-$C_{1-4}$haloalkyl, -O-$C_{1-6}$alkyl$NR^aR^a$, -O-$C_{1-6}$alkyl$R^c$, -O-$C_{1-6}$alkyl$OR^a$, -O-$C_{1-6}$alkylC(=O)$OR^a$, -$NR^aR^a$, -$NR^a$-$C_{1-4}$haloalkyl, -$NR^a$-$C_{1-6}$alkyl$NR^aR^a$, -$NR^a$-$C_{1-6}$alkyl$OR^a$, -C(=O)$C_{1-6}$alkyl, -C(=O)$OC_{1-6}$alkyl, -OC(=O)$C_{1-6}$alkyl, -C(=O)$NR^aC_{1-6}$alkyl or -$NR^a$C(=O)$C_{1-6}$alkyl; or R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^aR^a, -C_{1-6}alkylNR^aR^a, -C(=O)OR^a, -C(=O)NR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -OC(=O)C_{1-6}alkyl, -NR^aC(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, -C(=O)R^c or

$-C_{1-3}alkylR^c$; wherein if R^{10}, R^{12}, R^{13} and R^{14} are all H, then R^{11} is not $-O-C_{1-6}alkylNR^aR^a$ or $-O-C_{1-6}alkylOR^a$;

R^{12} is independently, at each instance, H, $C_{1-9}alkyl$, $-C_{1-3}alkylOR^a$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$; or R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

when R^1 is $4-C_{1-6}alkylphenyl$ or 2,4-dimethylphenyl, then R^{11} is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylR^c$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$; or R^{10} and R^{11} together are $-L^3-NR^a-$, respectively, or $-L^4-O-$, respectively; or R^{11} and R^{12} are $-NR^a-L^3-$, $-L^3-NR^a-$, $-O-L^4-$ or $-L^4-O-$; or R^{12} is $-NR^aR^b$; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, $C_{1-6}alkyl$ and $C_{1-3}haloalkyl$; and saturated carbon atoms may be additionally substituted by =O; or R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or

unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 1, 2 or 3 substituents independently selected from C_{2-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -$S(=O)_nC_{1-6}$alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -O-C_{1-6}alkylC(=O)OR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a, -NR^a-C_{1-6}alkylOR^a, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)NR^aC_{1-6}alkyl and -NR^aC(=O)C_{1-6}alkyl;

R^{13} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -$S(=O)_nC_{1-6}$alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -O-C_{1-6}alkylC(=O)OR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a, -NR^a-C_{1-6}alkylOR^a, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)NR^aC_{1-6}alkyl or -NR^aC(=O)C_{1-6}alkyl;

R^{14} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -$S(=O)_nC_{1-6}$alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^aR^a, -O-C_{1-6}alkylOR^a, -O-C_{1-6}alkylC(=O)OR^a, -NR^aR^a, -NR^a-C_{1-4}haloalkyl, -NR^a-C_{1-6}alkylNR^aR^a, -NR^a-C_{1-6}alkylOR^a, -C(=O)C_{1-6}alkyl, -C(=O)OC_{1-6}alkyl, -OC(=O)C_{1-6}alkyl, -C(=O)NR^aC_{1-6}alkyl or -NR^aC(=O)C_{1-6}alkyl;

R^a is independently, at each instance, H, phenyl, benzyl or C_{1-6}alkyl;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a;

R^c is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-3}haloalkyl, -OR^a and -NR^aR^a; or R^c is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-3}haloalkyl, -OR^a and -NR^aR^a;

L^1 is a bond, -CH_2CH_2- or -CH=CH-;

L^2 is NR^a, O, $S(=O)_n$, -N=CH-, $-CH_2NR^a-$, -CH=N- or $-NR^aCH_2-$;

L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

L^4 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0 or 1 atoms independently selected from O, N and S, wherein at least one of the carbon atoms in the bridge is substituted by =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OC_{1-6}alkyl$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

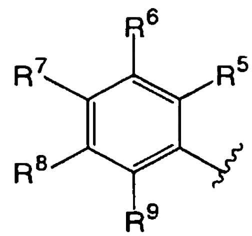
X is O, S or NR^a; or X and R^2 together are =N-CH=CH-, =C-O-, =C-S-, or $=C-NR^a-$;

Y is NH or O; and

n is independently, at each instance, 0, 1 or 2; with the proviso that when R^1 is 4-chlorophenyl, then R^4 is not 3-methoxyphenyl.

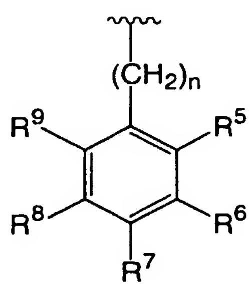
2. A compound according to Claim 1, wherein:

R^1 is



or a naphthyl or saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the naphthyl, heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^2 is H, hydroxy, halo, C_{1-6}alkyl substituted by 0, 1 or 2 substituents selected from R^{10},

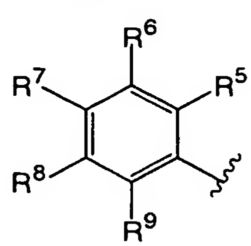


,

or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7; and

R^3 is H or C_{1-4}alkyl.

3. A compound according to Claim 1, wherein R^1 is



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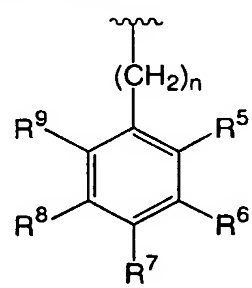
4. A compound according to Claim 3, wherein R^7 is independently, at each instance, C_{2-9}alkyl or C_{1-4}haloalkyl.

5. A compound according to Claim 1, wherein R^1 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

6. A compound according to Claim 5, wherein R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

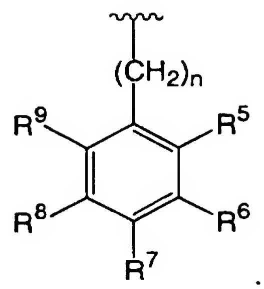
7. A compound according to Claim 2, wherein R^2 is



,

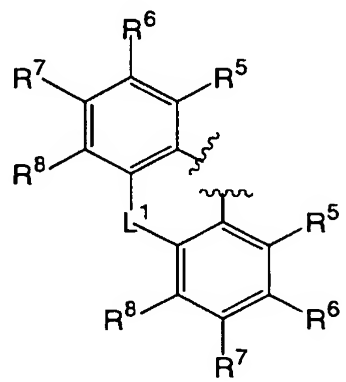
or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

8. A compound according to Claim 7, wherein R^2 is

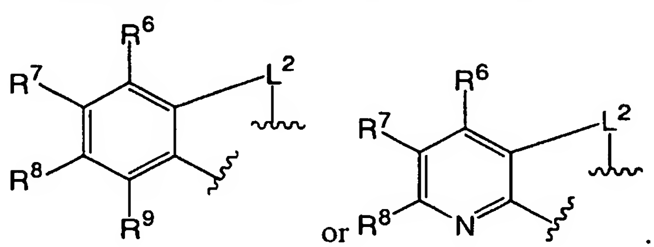


9. A compound according to Claim 7, wherein R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7.

10. A compound according to Claim 2, wherein R^1 and R^2 together are



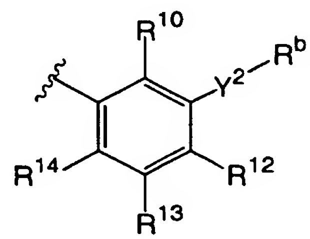
11. A compound according to Claim 2, wherein R^1 and R^3 together are



12. A compound according to Claim 2, wherein X and R^2 together are =N-CH=CH-, =C-O-, =C-S-, or =C-NR^a-.

13. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



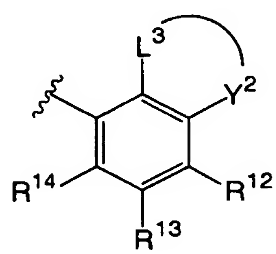
;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^a- or -O-.

14. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



;

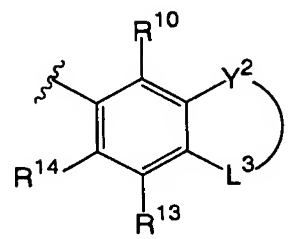
L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0 or 1 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^{a}R^a, -C_{1-6}alkylNR^{a}R^a, -C(=O)OR^a, -C(=O)NR^{a}R^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^{a}R^a, -OC(=O)C_{1-6}alkyl, -NR^{a}C(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^{a}C(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^{a}R^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^{a}R^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^{a}C(=O)C_{1-6}alkyl, -C(=O)R^c or -C_{1-3}alkylR^c;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^b- or -O-.

15. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



;

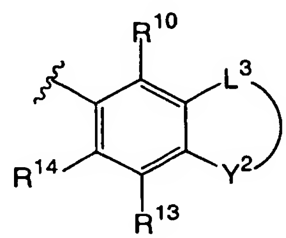
L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, -OR^a, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -NR^aR^a, -C_{1-6}alkylNR^aR^a, -C(=O)OR^a, -C(=O)NR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -OC(=O)C_{1-6}alkyl, -NR^aC(=O)C_{1-6}alkyl, -C_{1-3}alkylOC(=O)C_{1-6}alkyl or -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, and any nitrogen atoms in the bridge are substituted by H, -C_{1-6}alkylOR^a, -C_{1-6}alkyl, -C_{1-6}alkylNR^aR^a, -C_{1-3}alkylC(=O)OR^a, -C_{1-3}alkylC(=O)NR^aR^a, -C_{1-3}alkylOC(=O)C_{1-6}alkyl, -C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl, -C(=O)R^c or -C_{1-3}alkylR^c;

R^b is H, C_{1-6}alkyl, -C(=O)C_{1-6}alkyl, C_{1-6}alkyl-O-R^a; and

Y^2 is -NR^b- or -O-.

16. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



;

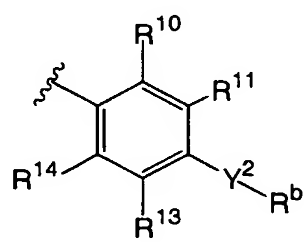
L^3 is a 2- or 3-atom, saturated or unsaturated, bridge containing 1, 2 or 3 carbon atoms and 0, 1 or 2 atoms independently selected from O, N and S, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $-OR^a$, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-NR^aR^a$, $-C_{1-6}alkylNR^aR^a$, $-C(=O)OR^a$, $-C(=O)NR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-OC(=O)C_{1-6}alkyl$, $-NR^aC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$ or $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^a$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^aR^a$, $-C_{1-3}alkylC(=O)OR^a$, $-C_{1-3}alkylC(=O)NR^aR^a$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^aC(=O)C_{1-6}alkyl$, $-C(=O)R^c$ or $-C_{1-3}alkylR^c$;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl-O-R^a$; and

Y^2 is $-NR^b-$ or -O-.

17. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



;

R^b is H, $C_{1-6}alkyl$, $-C(=O)C_{1-6}alkyl$, $C_{1-6}alkyl-O-R^a$; and

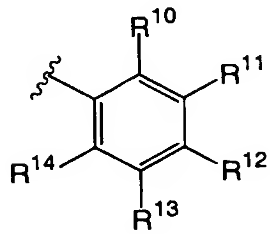
Y^2 is $-NR^a-$ or -O-.

18. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^a, NR^aR^a, $C_{1-6}alkyl$ and $C_{1-3}haloalkyl$; and saturated carbon atoms may be additionally substituted by =O.

19. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein:

R^4 is



;

R^{10} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl, -C(=O)OC$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{a}C$_{1-6}$alkyl or -NR^{a}C(=O)C$_{1-6}$alkyl;

R^{11} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylR^c, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl, -C(=O)OC$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{a}C$_{1-6}$alkyl or -NR^{a}C(=O)C$_{1-6}$alkyl;

C$_{1-6}$alkylNR^{a}R^a;

R^{12} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl, -C(=O)OC$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{a}C$_{1-6}$alkyl or -NR^{a}C(=O)C$_{1-6}$alkyl;

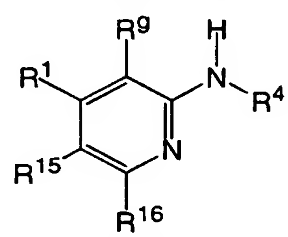
R^{13} is independently, at each instance, H, C_{1-9}alkyl, -C_{1-3}alkylOR^a, C_{1-4}haloalkyl, halo, nitro, cyano, -OR^a, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{a}R^a, -O-C$_{1-6}$alkylOR^a, -O-C$_{1-6}$alkylC(=O)OR^a, -NR^{a}R^a, -NR^a-C$_{1-4}$haloalkyl, -NR^a-C$_{1-6}$alkylNR^{a}R^a, -NR^a-C$_{1-6}$alkylOR^a, -C(=O)C$_{1-6}$alkyl,

$-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$; and

R^{14} is independently, at each instance, H, $C_{1-9}alkyl$, $-C_{1-3}alkylOR^a$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^a$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^aR^a$, $-O-C_{1-6}alkylOR^a$, $-O-C_{1-6}alkylC(=O)OR^a$, $-NR^aR^a$, $-NR^a-C_{1-4}haloalkyl$, $-NR^a-C_{1-6}alkylNR^aR^a$, $-NR^a-C_{1-6}alkylOR^a$, $-C(=O)C_{1-6}alkyl$, $-C(=O)OC_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^aC_{1-6}alkyl$ or $-NR^aC(=O)C_{1-6}alkyl$; wherein one of R^{10} and R^{12} is not H.

20. A compound according to any one of Claims 2, 4, 5, 8 or 9, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing ~~1, 2~~ or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, $C_{1-4}haloalkyl$, $-OR^a$ and $-NR^aR^a$.

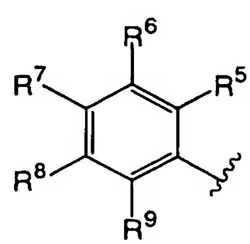
21. A compound having the structure:



or any pharmaceutically-acceptable salt thereof, wherein:

n is independently, at each instance, 0, 1 or 2.

R^1 is



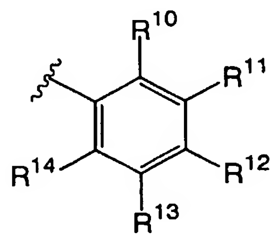
;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, -$(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}alkyl)C_{1-3}$alkyl or C_{1-3}alkyl;

R^4 is



; or

R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, oxo, -OR^d, -$S(=O)_nC_{1-6}$alkyl, -OC_{1-4}haloalkyl, -$OC_{2-6}alkylNR^dR^d$, -$OC_{2-6}alkylOR^d$, -$OC_{1-6}alkylC(=O)OR^d$, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -$NR^dC_{2-6}alkylNR^dR^d$, -$NR^dC_{2-6}alkylOR^d$, -$C(=O)C_{1-6}$alkyl, -$C(=O)OC_{1-6}$alkyl, -$OC(=O)C_{1-6}$alkyl, -$C(=O)NR^dC_{1-6}$alkyl and -$NR^dC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, -$C_{1-6}alkylOR^d$, -C_{1-6}alkyl, -$C_{1-6}alkylNR^dR^d$,

$-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$; or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, $C_{1-6}alkyl$ and $C_{1-3}haloalkyl$; and saturated carbon atoms may be additionally substituted by =O; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl;

R^5 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, naphthyl, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)R^d$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$, $-OC(=O)NR^dR^d$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(C_{1-6}alkyl)$, a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$ or $-S(C_{1-6}alkyl)$; or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, $C_{1-2}haloalkyl$ and $C_{1-3}alkyl$;

R^8 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d, -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d or -NR^dC_{2-6}alkylOR^d, -CO_2(C_{1-6}alkyl), -C(=O)(C_{1-6}alkyl), -C(=O)NR^dR^d, -NR^dC(=O)(C_{1-6}alkyl), -NR^dC(=O)NR^dR^d, -NR^dCO_2(C_{1-6}alkyl), -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d, -$S(=O)_n$(C_{1-6}alkyl), -$S(=O)_2NR^dR^d$, -$NR^dS(=O)_2$(C_{1-6}alkyl), -OC(=O)NR^dR^d, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -NR^dC_{1-4}haloalkyl, -NR^dC_{2-6}alkylNR^dR^d, -NR^dC_{2-6}alkylOR^d, -C_{1-8}alkylOR^d, -C_{1-6}alkylNR^dR^d or -S(C_{1-6}alkyl);

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^dR^d, -C(=NR^d)NR^dR^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^dR^d, -OC(=O)N(R^d)$S(=O)_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^dR^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -$S(=O)_2$(C_{1-8}alkyl), -$S(=O)_2NR^dR^d$, -$S(=O)_2N(R^d)$C(=O)(C_{1-8}alkyl), -$S(=O)_2N(R^d)$C(=O)O(C_{1-8}alkyl), -$S(=O)_2N(R^d)$C(=O)NR^dR^d, -NR^dR^d, -N(R^d)C(=O)(C_{1-8}alkyl),

$-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^{11} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$,

$-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{11} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{11} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$,

$-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$;

R^{12} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{12} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$,

$-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{12} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; wherein if R^{11} or R^{13} is CF_3, then R^{12} is not F; or R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$;

R^{13} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$,

$-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{13} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{13} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^{14} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$,

$-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{14} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{14} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^d is independently, at each instance, H, phenyl, benzyl or $C_{1-6}alkyl$;

R^e is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole,

1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-4-yl, 1,2,4-triazol-4-yl, 1,2,4-triazol-5-yl, isoxazol-3-yl, isoxazol-5-yl, pyrazol-3-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazoline, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,, 2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazole, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine, 1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine,

1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 2,3-dihydropyrimidine, 2,5-dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine,

1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1,2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-1,3,4-oxadiazine and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^f is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; or R^f is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; and

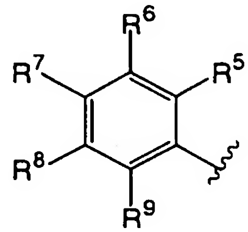
R^g is hydrogen or $-CH_3$.

22. The compound according to Claim 21, wherein R^{16} is halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl or C_{1-3}alkyl.

23. The compound according to Claim 21, wherein R^{10} is independently, at each instance, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$,

-OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{d}R^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{d}R^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{d}R^d, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^{d}R^d, -NR^{d}R^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^{d}R^d, -N(R^d)C(=NR^d)NR^{d}R^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2$NR^{d}R^d, -NR^dC_{2-6}alkylNR^{d}R^d and -NR^dC_{2-6}alkylOR^d; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{d}R^d, -C(=NR^d)NR^{d}R^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{d}R^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{d}R^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{d}R^d, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^{d}R^d, -NR^{d}R^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^{d}R^d, -N(R^d)C(=NR^d)NR^{d}R^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2$NR^{d}R^d, -NR^dC_{2-6}alkylNR^{d}R^d and -NR^dC_{2-6}alkylOR^d; or R^{10} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{d}R^d, -C(=NR^d)NR^{d}R^d, -OR^d, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{d}R^d, -OC(=O)N(R^d)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{d}R^d, -OC_{2-6}alkylOR^d, -SR^d, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{d}R^d, -S(=O)$_2$N(R^d)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^d)C(=O)NR^{d}R^d, -NR^{d}R^d, -N(R^d)C(=O)(C_{1-8}alkyl), -N(R^d)C(=O)O(C_{1-8}alkyl), -N(R^d)C(=O)NR^{d}R^d, -N(R^d)C(=NR^d)NR^{d}R^d, -N(R^d)S(=O)$_2$(C_{1-8}alkyl), -N(R^d)S(=O)$_2$NR^{d}R^d, -NR^dC_{2-6}alkylNR^{d}R^d and -NR^dC_{2-6}alkylOR^d.

24. The compound according to any one of Claim 21, wherein R^1 is



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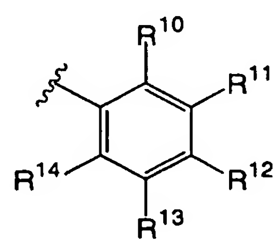
25. The compound according to Claim 24, wherein R^7 is C_{1-5}alkyl, halo or C_{1-4}haloalkyl.

26. The compound according to Claim 21, wherein R^1 is naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

27. The compound according to Claim 21, wherein R^1 is R^e substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

28. The compound according to Claim 27, wherein R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5.

29. The compound according to Claim 21, wherein R^4 is



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30. The compound according to Claim 29, wherein

R^{10} and R^{11} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl),

$-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$; or

R^{11} and R^{12} together are a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the each of the carbon atoms in the bridge is substituted by H, =O, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$, and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}alkylOR^d$, $-C_{1-6}alkyl$, $-C_{1-6}alkylNR^dR^d$, $-C_{1-3}alkylC(=O)OR^d$, $-C_{1-3}alkylC(=O)NR^dR^d$, $-C_{1-3}alkylOC(=O)C_{1-6}alkyl$, $-C_{1-3}alkylNR^dC(=O)C_{1-6}alkyl$, $-C(=O)R^f$ or $-C_{1-3}alkylR^f$.

31. The compound according to Claim 21, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with

the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, oxo, $-OR^d$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-OC_{1-6}$alkyl$C(=O)OR^d$, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^dC_{1-6}$alkyl and $-NR^dC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^d, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^dR^d, $-C_{1-3}$alkyl$C(=O)OR^d$, $-C_{1-3}$alkyl$C(=O)NR^dR^d$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^dC(=O)C_{1-6}$alkyl, $-C(=O)R^f$ or $-C_{1-3}$alkylR^f.

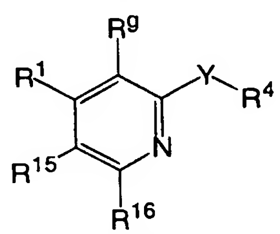
32. The compound according to Claim 31, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the heterocycle and bridge are substituted by 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, oxo, $-OR^d$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-OC_{1-6}$alkyl$C(=O)OR^d$, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^dC_{1-6}$alkyl and $-NR^dC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^d, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^dR^d, $-C_{1-3}$alkyl$C(=O)OR^d$, $-C_{1-3}$alkyl$C(=O)NR^dR^d$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^dC(=O)C_{1-6}$alkyl, $-C(=O)R^f$ or $-C_{1-3}$alkylR^f.

33. The compound according to Claim 21, wherein or R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 0, 1,

2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O.

34. The compound according to Claim 33, wherein R^4 is 10-membered bicyclic ring comprising fused 6-membered rings, containing 1, 2, 3 or 4 N atoms with the remainder being carbon atoms, with at least one of the 6-membered rings being aromatic, wherein the carbon atoms are substituted by H, halo, OR^d, NR^dR^d, C_{1-6}alkyl and C_{1-3}haloalkyl; and saturated carbon atoms may be additionally substituted by =O.

35. A compound having the structure:



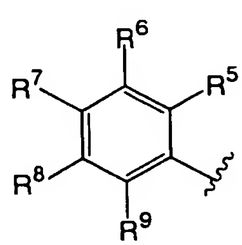
or any pharmaceutically-acceptable salt thereof, wherein:

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

Y is NH, O or S;

R^1 is



;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, -$(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, -NH_2, -NHC_{1-3}alkyl, -$N(C_{1-3}$alkyl$)C_{1-3}$alkyl or C_{1-3}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -$C(=O)R^n$, -$C(=O)OR^n$, -$C(=O)NR^mR^m$, -$C(=NR^m)NR^mR^m$, -OR^m, -$OC(=O)R^n$, -$OC(=O)NR^mR^m$, -$OC(=O)N(R^m)S(=O)_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -$S(=O)R^n$, -$S(=O)_2R^n$, -$S(=O)_2NR^mR^m$, -$S(=O)_2N(R^m)C(=O)R^n$, -$S(=O)_2N(R^m)C(=O)OR^n$, -$S(=O)_2N(R^m)C(=O)NR^mR^m$, -$NR^mR^m$, -$N(R^m)C(=O)R^n$, -$N(R^m)C(=O)OR^n$, -$N(R^m)C(=O)NR^mR^m$, -$N(R^m)C(=NR^m)NR^mR^m$, -$N(R^m)S(=O)_2R^n$, -$N(R^m)S(=O)_2NR^mR^m$, -$NR^mC_{2-6}$alkyl$NR^mR^m$, -$NR^mC_{2-6}$alkyl$OR^m$, -$C(=O)R^s$, -$C(=O)OR^s$, -$C(=O)NR^mR^s$, -$C(=NR^m)NR^mR^s$, -$OR^s$, -$OC(=O)R^s$, -$OC(=O)NR^mR^s$, -$OC(=O)N(R^m)S(=O)_2R^s$, -$OC_{2-6}$alkyl$NR^mR^s$, -$OC_{2-6}$alkyl$OR^s$, -$SR^s$, -$S(=O)R^s$, -$S(=O)_2R^s$, -$S(=O)_2NR^mR^s$, -$S(=O)_2N(R^m)C(=O)R^s$, -$S(=O)_2N(R^m)C(=O)OR^s$, -$S(=O)_2N(R^m)C(=O)NR^mR^s$, -$NR^mR^s$, -$N(R^m)C(=O)R^s$, -$N(R^m)C(=O)OR^s$, -$N(R^m)C(=O)NR^mR^s$, -$N(R^m)C(=NR^m)NR^mR^s$, -$N(R^m)S(=O)_2R^s$, -$N(R^m)S(=O)_2NR^mR^s$, -$NR^mC_{2-6}$alkyl$NR^mR^s$, -$NR^mC_{2-6}$alkyl$OR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -$C(=O)R^n$, -$C(=O)OR^n$, -$C(=O)NR^mR^m$, -$C(=NR^m)NR^mR^m$, -OR^m, -$OC(=O)R^n$, -$OC(=O)NR^mR^m$, -$OC(=O)N(R^m)S(=O)_2R^n$, -OC_{2-6}alkylNR^mR^m,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl;

R^5 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$, $-NR^dC_{2-6}alkylOR^d$, naphthyl, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)R^d$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$, $-OC(=O)NR^dR^d$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(C_{1-6}alkyl)$, a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$,

$-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C_{1-8}$alkylOR^d, $-C_{1-6}$alkylNR^dR^d or $-S(C_{1-6}$alkyl); or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^8 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C_{1-8}$alkylOR^d, $-C_{1-6}$alkylNR^dR^d, $-S(C_{1-6}$alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-NR^dR^d$, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d or $-NR^dC_{2-6}$alkylOR^d, $-CO_2(C_{1-6}$alkyl), $-C(=O)(C_{1-6}$alkyl), $-C(=O)NR^dR^d$, $-NR^dC(=O)(C_{1-6}$alkyl), $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}$alkyl), $-C_{1-8}$alkylOR^d, $-C_{1-6}$alkylNR^dR^d, $-S(=O)_n(C_{1-6}$alkyl), $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}$alkyl), $-OC(=O)NR^dR^d$ or a $-(CR^qR^q)_o$phenyl wherein the phenyl is substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is $-(CR^qR^q)_o$Het wherein Het is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^dR^d, $-OC_{2-6}$alkylOR^d, $-NR^dC_{1-4}$haloalkyl, $-NR^dC_{2-6}$alkylNR^dR^d, $-NR^dC_{2-6}$alkylOR^d, $-C_{1-8}$alkylOR^d, $-C_{1-6}$alkylNR^dR^d or $-S(C_{1-6}$alkyl);

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}$alkyl), $-C(=O)O(C_{1-8}$alkyl),

$-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$;

R^d is independently, at each instance, H, phenyl, benzyl or $C_{1-6}alkyl$;

R^e is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazole, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-4-yl, 1,2,4-triazol-4-yl, 1,2,4-triazol-5-yl, isoxazol-3-yl, isoxazol-5-yl, pyrazol-3-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazoline, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,, 2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazole, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine,

1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine, 1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 2,3-dihydropyrimidine, 2,5-

dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine, 1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1,2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-1,3,4-oxadiazine and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^f is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$; or R^f is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^d$ and $-NR^dR^d$;

R^g is hydrogen or $-CH_3$;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

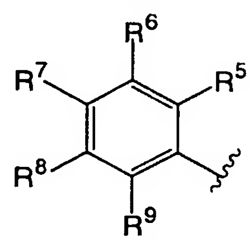
R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q.

36. The compound according to any one of Claim 35, wherein Y is NH.

37. The compound according to any one of Claim 35, wherein Y is O.

38. The compound according to any one of Claim 35, wherein Y is S.

39. The compound according to any one of Claim 35, wherein R^1 is



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40. The compound according to Claim 39, wherein R^7 is $C_{1-5}alkyl$, halo or $C_{1-4}haloalkyl$.

41. The compound according to Claim 35, wherein R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

42. The compound according to Claim 35, wherein R^1 is R^e substituted by 1, 2 or 3 substituents independently selected from R^5;

43. The compound according to Claim 35, wherein R^{15} is $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}.

44. The compound according to Claim 35, wherein R^{15} is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}.

45. The compound according to Claim 35, wherein R^{15} is C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}.

46. The compound according to Claim 35, wherein R^{15} is selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$,

$-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$; or R^{10} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^dR^d$, $-C(=NR^d)NR^dR^d$, $-OR^d$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^dR^d$, $-OC(=O)N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-SR^d$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^dR^d$, $-S(=O)_2N(R^d)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^d)C(=O)NR^dR^d$, $-NR^dR^d$, $-N(R^d)C(=O)(C_{1-8}alkyl)$, $-N(R^d)C(=O)O(C_{1-8}alkyl)$, $-N(R^d)C(=O)NR^dR^d$, $-N(R^d)C(=NR^d)NR^dR^d$, $-N(R^d)S(=O)_2(C_{1-8}alkyl)$, $-N(R^d)S(=O)_2NR^dR^d$, $-NR^dC_{2-6}alkylNR^dR^d$ and $-NR^dC_{2-6}alkylOR^d$.

47. The compound according to Claim 35, wherein R^{16} is, independently, in each instance, halo, $-NH_2$, $-NHC_{1-3}alkyl$, $-N(C_{1-3}alkyl)C_{1-3}alkyl$ or $C_{1-3}alkyl$.

48. The compound according to Claim 35, wherein R^4 is an unsaturated 6-membered ring containing 0 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$,

$-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

49. The compound according to Claim 35, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

50. The compound according to Claim 35, wherein R^4 is a saturated or unsaturated 6-membered ring containing 0 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and

bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

51. The compound according to Claim 35, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$,

$-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups; but in no instance is R^4 3,5-ditrifluoromethylphenyl or 3-trifluoromethyl-4-fluorophenyl.

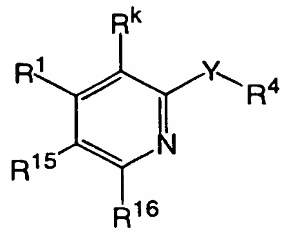
52. The compound according to Claim 35, wherein R^9 is H.

53. The compound according to Claim 35, wherein R^9 is independently, at each instance, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^dR^d$, $-OC_{2-6}alkylOR^d$, $-NR^dR^d$, $-NR^dC_{1-4}haloalkyl$, $-NR^dC_{2-6}alkylNR^dR^d$ or $-NR^dC_{2-6}alkylOR^d$, $-CO_2(C_{1-6}alkyl)$, $-C(=O)(C_{1-6}alkyl)$, $-C(=O)NR^dR^d$, $-NR^dC(=O)(C_{1-6}alkyl)$, $-NR^dC(=O)NR^dR^d$, $-NR^dCO_2(C_{1-6}alkyl)$, $-C_{1-8}alkylOR^d$, $-C_{1-6}alkylNR^dR^d$, $-S(=O)_n(C_{1-6}alkyl)$, $-S(=O)_2NR^dR^d$, $-NR^dS(=O)_2(C_{1-6}alkyl)$ or $-OC(=O)NR^dR^d$.

54. The compound according to Claim 35, wherein R^9 is a $-(CR^qR^q)_o$phenyl wherein the phenyl is substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}.

55. The compound according to Claim 35, wherein R^9 is $-(CR^qR^q)_o$Het wherein Het is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, $C_{1-2}haloalkyl$ and $C_{1-3}alkyl$.

56. A compound having the structure:

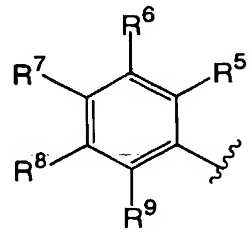


or any pharmaceutically-acceptable salt thereof, wherein:

Y is O or S;

n is independently, at each instance, 0, 1 or 2.

R^1 is



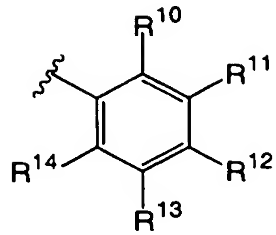
;

or R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5; or R^1 is R^i substituted by 1, 2 or 3 substituents independently selected from R^5;

R^{15} is, independently, in each instance, R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, the heterocycle and bridge being substituted by 0, 1, 2 or 3 substituents independently selected from R^{10};

R^{16} is, independently, in each instance, H, halo, $-NH_2$, $-NHC_{1-3}$alkyl, $-N(C_{1-3}alkyl)C_{1-3}$alkyl, $-OC_{1-3}$alkyl, $-C_{1-2}$haloalkyl, $-OC_{1-2}$haloalkyl or C_{1-3}alkyl;

R^4 is



;

wherein when R^1 is bromophenyl, methylphenyl or trifluoromethylphenyl, R^4 is not trifluoromethylphenyl or trifluoromethylhalophenyl; or R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-OC_{1-6}alkylC(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and each of the available nitrogen atoms in the heterocycle are substituted by H, $-C_{1-6}alkylOR^h$, $-C_{1-6}$alkyl, $-C_{1-6}alkylNR^hR^h$, $-C_{1-3}alkylC(=O)OR^h$, $-C_{1-3}alkylC(=O)NR^hR^h$, $-C_{1-3}alkylOC(=O)C_{1-6}$alkyl, $-C_{1-3}alkylNR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}alkylR^j$; or R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 0, 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms selected from S and O with the remainder being carbon atoms, wherein each of the carbon atoms of the ring is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-OC_{1-6}alkylC(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the ring are substituted by H, $-C_{1-6}alkylOR^h$, $-C_{1-6}$alkyl, $-C_{1-6}alkylNR^hR^h$, $-C_{1-3}alkylC(=O)OR^h$, $-C_{1-3}alkylC(=O)NR^hR^h$, $-C_{1-3}alkylOC(=O)C_{1-6}$alkyl, $-C_{1-3}alkylNR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}alkylR^j$;

R^5 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, nitro, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, naphthyl, -$CO_2(C_{1-6}$alkyl), -C(=O)(C_{1-6}alkyl), -C(=O)NR^hR^h, -$NR^hC(=O)R^h$, -$NR^hC(=O)NR^hR^h$, -$NR^hCO_2(C_{1-6}$alkyl), -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^hR^h, -$S(=O)_n(C_{1-6}$alkyl), -$S(=O)_2NR^hR^h$, -$NR^hS(=O)_2(C_{1-6}$alkyl), -OC(=O)NR^hR^h, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^5 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^6 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h or -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^hR^h, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}; or R^6 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^7 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, bromo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^hR^h or -S(C_{1-6}alkyl); or R^7 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^8 is independently, at each instance, H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^hR^h, -S(C_{1-6}alkyl), a phenyl ring substituted with 1, 2, or 3 substituents independently selected from R^{10}, or R^8 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10};

R^9 is independently, at each instance, H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, nitro, $-OC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h or $-NR^hC_{2-6}$alkylOR^h, $-CO_2(C_{1-6}$alkyl), $-C(=O)(C_{1-6}$alkyl), $-C(=O)NR^hR^h$, $-NR^hC(=O)(C_{1-6}$alkyl), $-NR^hC(=O)NR^hR^h$, $-NR^hCO_2(C_{1-6}$alkyl), $-C_{1-8}$alkylOR^h, $-C_{1-6}$alkylNR^hR^h, $-S(=O)_n(C_{1-6}$alkyl), $-S(=O)_2NR^hR^h$, $-NR^hS(=O)_2(C_{1-6}$alkyl), $-OC(=O)NR^hR^h$, a phenyl ring substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; or R^9 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S substituted with 0, 1, 2, or 3 substituents independently selected from R^{10}; wherein at least one of R^5, R^6, R^7, R^8 and R^9 is C_{1-8}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C_{1-8}$alkylOR^h, $-C_{1-6}$alkylNR^hR^h or $-S(C_{1-6}$alkyl); or R^9 is a saturated or unsaturated 4- or 5-membered ring heterocycle containing a single nitrogen atom, wherein the ring is substituted with 0, 1 or 2 substituents independently selected from halo, C_{1-2}haloalkyl and C_{1-3}alkyl;

R^{10} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}$alkyl), $-C(=O)O(C_{1-8}$alkyl), $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}$alkyl), $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}$alkyl), $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-SR^h$, $-S(=O)(C_{1-8}$alkyl), $-S(=O)_2(C_{1-8}$alkyl), $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}$alkyl), $-S(=O)_2N(R^h)C(=O)O(C_{1-8}$alkyl), $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}$alkyl), $-N(R^h)C(=O)O(C_{1-8}$alkyl), $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}$alkyl), $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}$alkylNR^hR^h and $-NR^hC_{2-6}$alkylOR^h; or R^{10} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1 or 2 atoms selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O

and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^hR^h$, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2NR^hR^h$, -NR^hC_{2-6}alkylNR^hR^h and -NR^hC_{2-6}alkylOR^h; or R^{10} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^hR^h$, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2NR^hR^h$, -NR^hC_{2-6}alkylNR^hR^h and -NR^hC_{2-6}alkylOR^h;

R^{11} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2NR^hR^h$, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2NR^hR^h$, -NR^hC_{2-6}alkylNR^hR^h and -NR^hC_{2-6}alkylOR^h; or R^{11} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo

groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{11} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h;

R^{12} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{12} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3

atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{12} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h;

R^{13} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{13} is a saturated or unsaturated 5-, 6- or 7-membered

monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1, 2 or 3 atoms selected from N, O and S, wherein the ring is fused with 0 or 1 benzo groups and 0 or 1 saturated or unsaturated 5-, 6- or 7-membered heterocyclic ring containing 1, 2 or 3 atoms selected from N, O and S; wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h; or R^{13} is C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and -NR^hC_{2-6}alkylOR^h;

R^{14} is independently, at each instance, selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^{h}R^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^hC_{2-6}alkylNR^{h}R^h and

-NR^{h}C$_{2-6}$alkylOR^h; or R^{14} is a saturated or unsaturated 5-, 6- or 7-membered monocyclic or 6-, 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 1 or 2 atoms selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 groups selected from C$_{1-8}$alkyl, C$_{1-4}$haloalkyl, halo, cyano, nitro, -C(=O)(C$_{1-8}$alkyl), -C(=O)O(C$_{1-8}$alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C$_{1-8}$alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C$_{1-8}$alkyl), -OC$_{2-6}$alkylNR^{h}R^h, -OC$_{2-6}$alkylOR^h, -SR^h, -S(=O)(C$_{1-8}$alkyl), -S(=O)$_2$(C$_{1-8}$alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C$_{1-8}$alkyl), -S(=O)$_2$N(R^h)C(=O)O(C$_{1-8}$alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C$_{1-8}$alkyl), -N(R^h)C(=O)O(C$_{1-8}$alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C$_{1-8}$alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^{h}C$_{2-6}$alkylNR^{h}R^h and -NR^{h}C$_{2-6}$alkylOR^h; or R^{14} is C$_{1-4}$alkyl substituted by 0, 1, 2 or 3 groups selected from C$_{1-4}$haloalkyl, halo, cyano, nitro, -C(=O)(C$_{1-8}$alkyl), -C(=O)NR^{h}R^h, -C(=NR^h)NR^{h}R^h, -OR^h, -OC(=O)(C$_{1-8}$alkyl), -OC(=O)NR^{h}R^h, -OC(=O)N(R^h)S(=O)$_2$(C$_{1-8}$alkyl), -OC$_{2-6}$alkylNR^{h}R^h, -OC$_{2-6}$alkylOR^h, -SR^h, -S(=O)(C$_{1-8}$alkyl), -S(=O)$_2$(C$_{1-8}$alkyl), -S(=O)$_2$NR^{h}R^h, -S(=O)$_2$N(R^h)C(=O)(C$_{1-8}$alkyl), -S(=O)$_2$N(R^h)C(=O)O(C$_{1-8}$alkyl), -S(=O)$_2$N(R^h)C(=O)NR^{h}R^h, -NR^{h}R^h, -N(R^h)C(=O)(C$_{1-8}$alkyl), -N(R^h)C(=O)O(C$_{1-8}$alkyl), -N(R^h)C(=O)NR^{h}R^h, -N(R^h)C(=NR^h)NR^{h}R^h, -N(R^h)S(=O)$_2$(C$_{1-8}$alkyl), -N(R^h)S(=O)$_2$NR^{h}R^h, -NR^{h}C$_{2-6}$alkylNR^{h}R^h and -NR^{h}C$_{2-6}$alkylOR^h;

R^h is independently, at each instance, H, phenyl, benzyl or C$_{1-6}$alkyl, the phenyl, benzyl and C$_{1-6}$alkyl being substituted by 0, 1, 2 or 3 substituents selected from halo, C$_{1-4}$alkyl, C$_{1-3}$haloalkyl, -OC$_{1-4}$alkyl, -NH$_2$, -NHC$_{1-4}$alkyl, -N(C$_{1-4}$alkyl)C$_{1-4}$alkyl;

R^i is a heterocycle selected from the group of thiophene, pyrrole, 1,3-oxazole, 1,3-thiazol-5-yl, 1,3,4-oxadiazole, 1,3,4-thiadiazole, 1,2,3-oxadiazole, 1,2,3-thiadiazole, 1H-1,2,3-triazole, isothiazole, 1,2,4-oxadiazole, 1,2,4-

thiadiazole, 1,2,3,4-oxatriazole, 1,2,3,4-thiatriazole, 1H-1,2,3,4-tetraazole, 1,2,3,5-oxatriazole, 1,2,3,5-thiatriazole, furan, imidazol-1-yl, imidazol-3-yl, imidazol-4-yl, 1,2,4-triazole, 1,2,4-triazole, isoxazole, pyrazol-3-yl, pyrazol-4-yl, pyrazol-5-yl, thiolane, pyrrolidine, tetrahydrofuran, 4,5-dihydrothiophene, 2-pyrroline, 4,5-dihydrofuran, pyridazine, pyrimidine, pyrazine, 1,2,3-triazine, 1,2,4-triazine, 1,2,4-triazine, 1,3,5-triazine, pyridine, 2H-3,4,5,6-tetrahydropyran, thiane, 1,2-diazaperhydroine, 1,3-diazaperhydroine, piperazine, 1,3-oxazaperhydroine, morpholine, 1,3-thiazaperhydroine, 1,4-thiazaperhydroine, piperidine, 2H-3,4-dihydropyran, 2,3-dihydro-4H-thiin, 1,4,5,6-tetrahydropyridine, 2H-5,6-dihydropyran, 2,3-dihydro-6H-thiin, 1,2,5,6-tetrahydropyridine, 3,4,5,6-tetrahydropyridine, 4H-pyran, 4H-thiin, 1,4-dihydropyridine, 1,4-dithiane, 1,4-dioxane, 1,4-oxathiane, 1,2-oxazolidine, 1,2-thiazolidine, pyrazolidine, 1,3-oxazolidine, 1,3-thiazolidine, imidazolidine, 1,2,4-oxadiazolidine, 1,3,4-oxadiazolidine, 1,2,4-thiadiazolidine, 1,3,4-thiadiazolidine, 1,2,4-triazolidine, 2-imidazolin-1-yl, 2-imidazolin-2-yl, 2-imidazolin-5-yl, 3-imidazoline, 2-pyrazoline, 4-imidazoline, 2,3-dihydroisothiazole, 4,5-dihydroisoxazole, 4,5-dihydroisothiazole, 2,5-dihydroisoxazole, 2,5-dihydroisothiazole, 2,3-dihydroisoxazole, 4,5-dihydrooxazole, 2,3-dihydrooxazole, 2,5-dihydrooxazole, 4,5-dihydrothiazole, 2,3-dihydrothiazole,, 2,5-dihydrothiazole, 1,3,4-oxathiazolidine, 1,4,2-oxathiazolidine, 2,3-dihydro-1H-[1,2,3]triazole, 2,5-dihydro-1H-[1,2,3]triazole, 4,5-dihydro-1H-[1,2,3]triazol-1-yl, 4,5-dihydro-1H-[1,2,3]triazol-3-yl, 4,5-dihydro-1H-[1,2,3]triazol-5-yl, 2,3-dihydro-1H-[1,2,4]triazole, 4,5-dihydro-1H-[1,2,4]triazole, 2,3-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thidiazole, 2,5-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,5-dihydro-[1,2,4]oxadiazole, 2,3-dihydro-[1,2,4]oxadiazole, 4,5-dihydro-[1,2,4]oxadiazole, 2,5-dihydro-[1,2,4]thiadiazole, 2,3-dihydro-[1,2,4] thiadiazole, 4,5-dihydro-[1,2,4] thiadiazole, 2,3-dihydro-[1,3,4]oxadiazole, 2,3-dihydro-[1,3,4]thiadiazole, [1,4,2]oxathiazole, [1,3,4]oxathiazole, 1,3,5-triazaperhydroine, 1,2,4-triazaperhydroine, 1,4,2-dithiazaperhydroine, 1,4,2-dioxazaperhydroine, 1,3,5-oxadiazaperhydroine, 1,2,5-oxadiazaperhydroine, 1,3,4-thiadiazaperhydroine, 1,3,5-thiadiazaperhydroine, 1,2,5-

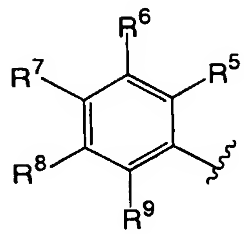
thiadiazaperhydroine, 1,3,4-oxadiazaperhydroine, 1,4,3-oxathiazaperhydroine, 1,4,2-oxathiazaperhydroine, 1,4,5,6-tetrahydropyridazine, 1,2,3,4-tetrahydropyridazine, 1,2,3,6-tetrahydropyridazine, 1,2,5,6-tetrahydropyrimidine, 1,2,3,4-tetrahydropyrimidine, 1,4,5,6-tetrahydropyrimidine, 1,2,3,6-tetrahydropyrazine, 1,2,3,4-tetrahydropyrazine, 5,6-dihydro-4H-[1,2]oxazine, 5,6-dihydro-2H-[1,2]oxazine, 3,6-dihydro-2H-[1,2]oxazine, 3,4-dihydro-2H-[1,2]oxazine, 5,6-dihydro-4H-[1,2]thiazine, 5,6-dihydro-2H-[1,2] thiazine, 3,6-dihydro-2H-[1,2] thiazine, 3,4-dihydro-2H-[1,2] thiazine, 5,6-dihydro-2H-[1,3]oxazine, 5,6-dihydro-4H-[1,3]oxazine, 3,6-dihydro-2H-[1,3]oxazine, 3,4-dihydro-2H-[1,3]oxazine, 3,6-dihydro-2H-[1,4]oxazine, 3,4-dihydro-2H-[1,4]oxazine, 5,6-dihydro-2H-[1,3]thiazine, 5,6-dihydro-4H-[1,3]thiazine, 3,6-dihydro-2H-[1,3]thiazine, 3,4-dihydro-2H-[1,3]thiazine, 3,6-dihydro-2H-[1,4]thiazine, 3,4-dihydro-2H-[1,4]thiazine, 1,2,3,6-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,2,4]triazine, 1,2,3,4-tetrahydro-[1,3,5]triazine, 2,3,4,5-tetrahydro-[1,2,4]triazine, 1,4,5,6-tetrahydro-[1,2,4]triazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dioxazine, 5,6-dihydro-[1,4,2]dithiazine, 2,3-dihydro-[1,4,2]dioxazine, 3,4-dihydro-2H-[1,3,4]oxadiazine, 3,6-dihydro-2H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,3,5]oxadiazine, 3,6-dihydro-2H-[1,3,5]oxadiazine, 5,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,2,5]oxadiazine, 3,4-dihydro-2H-[1,3,4]thiadiazine, 3,6-dihydro-2H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,3,5]thiadiazine, 3,6-dihydro-2H-[1,3,5]thiadiazine, 5,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,2,5]thiadiazine, 5,6-dihydro-2H-[1,2,3]oxadiazine, 3,6-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-4H-[1,3,4]oxadiazine, 3,4-dihydro-2H-[1,2,5]oxadiazine, 5,6-dihydro-2H-[1,2,3]thiadiazine, 3,6-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-4H-[1,3,4]thiadiazine, 3,4-dihydro-2H-[1,2,5]thiadiazine, 5,6-dihydro-[1,4,3]oxathiazine, 5,6-dihydro-[1,4,2]oxathiazine, 2,3-dihydro-[1,4,3]oxathiazine, 2,3-dihydro-[1,4,2]oxathiazine, 4,5-dihydropyridine, 1,6-dihydropyridine, 5,6-dihydropyridine, 2H-pyran, 2H-thiin, 3,6-dihydropyridine, 2,3-dihydropyridazine, 2,5-dihydropyridazine, 4,5-dihydropyridazine, 1,2-dihydropyridazine, 1,4-dihydropyrimidin-1-yl, 1,4-dihydropyrimidin-4-yl, 1,4-dihydropyrimidin-5-yl, 1,4-dihydropyrimidin-6-yl,

2,3-dihydropyrimidine, 2,5-dihydropyrimidine, 5,6-dihydropyrimidine, 3,6-dihydropyrimidine, 4,5-dihydropyrazine, 5,6-dihydropyrazine, 3,6-dihydropyrazine, 4,5-dihydropyrazine, 1,4-dihydropyrazine, 1,4-dithiin, 1,4-dioxin, 2H-1,2-oxazine, 6H-1,2-oxazine, 4H-1,2-oxazine, 2H-1,3-oxazine, 4H-1,3-oxazine, 6H-1,3-oxazine, 2H-1,4-oxazine, 4H-1,4-oxazine, 2H-1,3-thiazine, 2H-1,4-thiazine, 4H-1,2-thiazine, 6H-1,3-thiazine, 4H-1,4-thiazine, 2H-1,2-thiazine, 6H-1,2-thiazine, 1,4-oxathiin, 2H,5H-1,2,3-triazine, 1H,4H-1,2,3-triazine, 4,5-dihydro-1,2,3-triazine, 1H,6H-1,2,3-triazine, 1,2-dihydro-1,2,3-triazine, 2,3-dihydro-1,2,4-triazine, 3H,6H-1,2,4-triazine, 1H,6H-1,2,4-triazine, 3,4-dihydro-1,2,4-triazine, 1H,4H-1,2,4-triazine, 5,6-dihydro-1,2,4-triazine, 4,5-dihydro-1,2,4-triazine, 2H,5H-1,2,4-triazine, 1,2-dihydro-1,2,4-triazine, 1H,4H-1,3,5-triazine, 1,2-dihydro-1,3,5-triazine, 1,4,2-dithiazine, 1,4,2-dioxazine, 2H-1,3,4-oxadiazine, 2H-1,3,5-oxadiazine, 6H-1,2,5-oxadiazine, 4H-1,3,4-oxadiazine, 4H-1,3,5-oxadiazine, 4H-1,2,5-oxadiazine, 2H-1,3,5-thiadiazine, 6H-1,2,5-thiadiazine, 4H-1,3,4-thiadiazine, 4H-1,3,5-thiadiazine, 4H-1,2,5-thiadiazine, 2H-1,3,4-thiadiazine, 6H-1,3,4-thiadiazine, 6H-1,3,4-oxadiazine, and 1,4,2-oxathiazine, wherein the heterocycle is optionally vicinally fused with a saturated or unsaturated 5-, 6- or 7-membered ring containing 0, 1 or 2 atoms independently selected from N, O and S;

R^j is phenyl substituted by 0, 1 or 2 groups selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^h$ and $-NR^hR^h$; or R^j is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the carbon atoms of the heterocycle are substituted by 0, 1 or 2 oxo groups, wherein the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents selected from halo, C_{1-4}alkyl, C_{1-3}haloalkyl, $-OR^h$ and $-NR^hR^h$; and

R^k is hydrogen or $-CH_3$.

57. The compound according to Claim 56, wherein R^1 is



58. The compound according to Claim 56, wherein R^7 is C_{2-6}alkyl or C_{1-4}haloalkyl.

59. The compound according to Claim 56, wherein R^1 is a naphthyl substituted by 0, 1, 2 or 3 substituents independently selected from R^5.

60. The compound according to Claim 56, wherein R^1 is R^i substituted by 1, 2 or 3 substituents independently selected from R^5.

61. The compound according to Claim 60, wherein R^i is substituted by one substituent selected from halo, C_{1-4}haloalkyl and C_{1-5}alkyl, and additionally by 0, 1 or 2 substituents independently selected from R^5.

62. The compound according to Claim 56, wherein R^{15} is H.

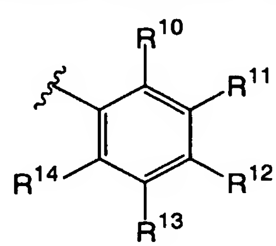
63. The compound according to Claim 56, wherein R^{15} is R^{10}, C_{1-8}alkyl substituted by 0, 1 or 2 substituents selected from R^{10}, or a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, the heterocycle and bridge being substituted by 0, 1, 2 or 3 substituents independently selected from R^{10}; or R^{15} is $-(CH_2)_n$phenyl substituted by 0, 1, 2 or 3 substituents independently selected from H, C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OC(=O)(C_{1-8}alkyl)$,

-OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, -S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^hR^h, -N$R^h$$C_{2-6}$alkylN$R^hR^h$, -N$R^h$$C_{2-6}$alkylO$R^h$, and C_{1-4}alkyl substituted by 0, 1, 2 or 3 groups selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)(C_{1-8}alkyl), -C(=O)O(C_{1-8}alkyl), -C(=O)NR^hR^h, -C(=NR^h)NR^hR^h, -OR^h, -OC(=O)(C_{1-8}alkyl), -OC(=O)NR^hR^h, -OC(=O)N(R^h)S(=O)$_2$(C_{1-8}alkyl), -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -SR^h, -S(=O)(C_{1-8}alkyl), -S(=O)$_2$(C_{1-8}alkyl), -S(=O)$_2$NR^hR^h, ~~-S(=O)$_2$N(R^h)C(=O)(C_{1-8}alkyl), -S(=O)$_2$N(R^h)C(=O)O(C_{1-8}alkyl),~~ -S(=O)$_2$N(R^h)C(=O)NR^hR^h, -NR^hR^h, -N(R^h)C(=O)(C_{1-8}alkyl), -N(R^h)C(=O)O(C_{1-8}alkyl), -N(R^h)C(=O)NR^hR^h, -N(R^h)C(=NR^h)NR^hR^h, -N(R^h)S(=O)$_2$(C_{1-8}alkyl), -N(R^h)S(=O)$_2$NR^hR^h, -N$R^h$$C_{2-6}$alkylN$R^hR^h$ and -N$R^h$$C_{2-6}$alkylO$R^h$.

64. The compound according to Claim 56, wherein R^{16} is H.

65. The compound according to Claim 56, wherein R^{16} is halo, -NHC_{1-3}alkyl, -N(C_{1-3}alkyl)C_{1-3}alkyl, -OC_{1-3}alkyl, -C_{1-2}haloalkyl, -OC_{1-2}haloalkyl or C_{1-3}alkyl.

66. The compound according to Claim 56, wherein R^4 is



;

wherein at least one of R^{10}, R^{11}, R^{12}, R^{13} and R^{14} is other than C_{1-4}haloalkyl or halo.

67. The compound according to Claim 66, wherein at least one of R^{10}, R^{11}, R^{12}, R^{13} and R^{14} is $-OR^h$ or $-NR^hR^h$.

68. The compound according to Claim 56, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the heterocycle are substituted by H, $-C_{1-6}$alkylOR^h, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^hR^h, $-C_{1-3}$alkyl$C(=O)OR^h$, $-C_{1-3}$alkyl$C(=O)NR^hR^h$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}$alkylR^j.

69. The compound according to Claim 56, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1 or 2 atoms selected from O, N and S, wherein each of the carbon atoms of the heterocycle is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, $-OR^h$, $-S(=O)_nC_{1-6}$alkyl, $-OC_{1-4}$haloalkyl, $-OC_{2-6}$alkylNR^hR^h, $-OC_{2-6}$alkylOR^h, $-OC_{1-6}$alkyl$C(=O)OR^h$, $-NR^hR^h$, $-NR^hC_{1-4}$haloalkyl, $-NR^hC_{2-6}$alkylNR^hR^h, $-NR^hC_{2-6}$alkylOR^h, $-C(=O)C_{1-6}$alkyl, $-C(=O)OC_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^hC_{1-6}$alkyl or $-NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the bridge are substituted by H, $-C_{1-6}$alkylOR^h, $-C_{1-6}$alkyl, $-C_{1-6}$alkylNR^hR^h, $-C_{1-3}$alkyl$C(=O)OR^h$, $-C_{1-3}$alkyl$C(=O)NR^hR^h$, $-C_{1-3}$alkyl$OC(=O)C_{1-6}$alkyl, $-C_{1-3}$alkyl$NR^hC(=O)C_{1-6}$alkyl, $-C(=O)R^j$ or $-C_{1-3}$alkylR^j.

70. The compound according to Claim 56, wherein R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms

selected from S and O with the remainder being carbon atoms, wherein each of the carbon atoms of the ring is substituted by H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, -OR^h, -$S(=O)_nC_{1-6}$alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -OC_{1-6}alkyl$C(=O)OR^h$, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, -$C(=O)C_{1-6}$alkyl, -$C(=O)OC_{1-6}$alkyl, -$OC(=O)C_{1-6}$alkyl, -$C(=O)NR^hC_{1-6}$alkyl or -$NR^hC(=O)C_{1-6}$alkyl; and saturated carbon atoms may be additionally substituted by =O; and any available nitrogen atoms in the ring are substituted by H, -C_{1-6}alkylOR^h, -C_{1-6}alkyl, -C_{1-6}alkylNR^hR^h, -C_{1-3}alkyl$C(=O)OR^h$, -C_{1-3}alkyl$C(=O)NR^hR^h$, -C_{1-3}alkyl$OC(=O)C_{1-6}$alkyl, -C_{1-3}alkyl$NR^hC(=O)C_{1-6}$alkyl, -$C(=O)R^j$ or -C_{1-3}alkylR^j.

71. The compound according to Claim 56, wherein R^4 is an 8-, 9-, 10- or 11-membered bicyclic ring, containing 0, 1, 2, 3 or 4 N atoms and 0, 1 or 2 atoms selected from S and O with the remainder being carbon atoms, wherein at least one of the carbon atoms of the ring is substituted by C_{1-9}alkyl, C_{1-4}haloalkyl, halo, cyano, oxo, -OR^h, -$S(=O)_nC_{1-6}$alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -OC_{1-6}alkyl$C(=O)OR^h$, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, -$C(=O)C_{1-6}$alkyl, -$C(=O)OC_{1-6}$alkyl, -$OC(=O)C_{1-6}$alkyl, -$C(=O)NR^hC_{1-6}$alkyl or -$NR^hC(=O)C_{1-6}$alkyl.

72. The compound according to Claim 56, wherein R^5 and R^9 are each independently selected from H, C_{1-4}haloalkyl, halo, nitro, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl, -NR^hC_{2-6}alkylNR^hR^h, -NR^hC_{2-6}alkylOR^h, -$CO_2(C_{1-6}$alkyl), -$C(=O)(C_{1-6}$alkyl), -$C(=O)NR^hR^h$, -$NR^hC(=O)R^h$, -$NR^hC(=O)NR^hR^h$, -$NR^hCO_2(C_{1-6}$alkyl), -C_{1-8}alkylOR^h, -C_{1-6}alkylNR^hR^h, -$S(=O)_n(C_{1-6}$alkyl), -$S(=O)_2NR^hR^h$, -$NR^hS(=O)_2(C_{1-6}$alkyl) and -$OC(=O)NR^hR^h$.

73. The compound according to Claim 56, wherein R^6 and R^8 are each independently selected from H, C_{1-5}alkyl, C_{1-4}haloalkyl, halo, -OC_{1-6}alkyl, -OC_{1-4}haloalkyl, -OC_{2-6}alkylNR^hR^h, -OC_{2-6}alkylOR^h, -NR^hR^h, -NR^hC_{1-4}haloalkyl,

$-NR^hC_{2-6}alkylNR^hR^h$ or $-NR^hC_{2-6}alkylOR^h$, $-C_{1-8}alkylOR^h$, $-C_{1-6}alkylNR^hR^h$ and $-S(C_{1-6}alkyl)$.

74. The compound according to Claim 56, wherein R^7 is independently, at each instance, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, $-OC_{1-4}haloalkyl$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-NR^hR^h$, $-NR^hC_{1-4}haloalkyl$, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$, $-C_{1-8}alkylOR^h$, $-C_{1-6}alkylNR^hR^h$ or $-S(C_{1-6}alkyl)$.

75. The compound according to Claim 56, wherein R^{10} and R^{14} are each independently selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$ and $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

76. The compound according to Claim 56, wherein R^{11} and R^{13} are independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$,

$-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$, $-NR^hC_{2-6}alkylOR^h$ and $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

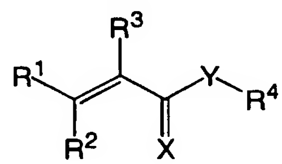
77. The compound according to Claim 56, wherein R^{12} is independently, at each instance, selected from H, $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$, $-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$; or R^{12} is $C_{1-4}alkyl$ substituted by 0, 1, 2 or 3 groups selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)(C_{1-8}alkyl)$, $-C(=O)O(C_{1-8}alkyl)$, $-C(=O)NR^hR^h$, $-C(=NR^h)NR^hR^h$, $-OR^h$, $-OC(=O)(C_{1-8}alkyl)$, $-OC(=O)NR^hR^h$, $-OC(=O)N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-OC_{2-6}alkylNR^hR^h$, $-OC_{2-6}alkylOR^h$, $-SR^h$, $-S(=O)(C_{1-8}alkyl)$, $-S(=O)_2(C_{1-8}alkyl)$, $-S(=O)_2NR^hR^h$,

$-S(=O)_2N(R^h)C(=O)(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)O(C_{1-8}alkyl)$, $-S(=O)_2N(R^h)C(=O)NR^hR^h$, $-NR^hR^h$, $-N(R^h)C(=O)(C_{1-8}alkyl)$, $-N(R^h)C(=O)O(C_{1-8}alkyl)$, $-N(R^h)C(=O)NR^hR^h$, $-N(R^h)C(=NR^h)NR^hR^h$, $-N(R^h)S(=O)_2(C_{1-8}alkyl)$, $-N(R^h)S(=O)_2NR^hR^h$, $-NR^hC_{2-6}alkylNR^hR^h$ and $-NR^hC_{2-6}alkylOR^h$.

78. The compound according to Claim 56, wherein Y is O.

79. The compound according to Claim 56, wherein Y is S.

80. A compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance $C_{1-8}alkyl$, phenyl or benzyl;

R^q is independently in each instance H, $C_{1-4}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

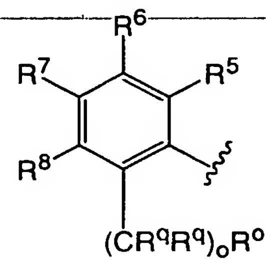
R^3 is H or $C_{1-4}alkyl$;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m, -NR^m-C_{1-6}alkylOR^m, or -$(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m; and

(A) R^1 is



R^2 is H, -OR^m, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2NR^mR^m$, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2NR^mR^m$, -NR^mC_{2-6}alkylNR^mR^m, -NR^mC_{2-6}alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^mR^s, -C(=NR^m)NR^mR^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^mR^s, -OC(=O)N(R^m)S(=O)$_2R^s$, -OC_{2-6}alkylNR^mR^s, -OC_{2-6}alkylOR^s,

$-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

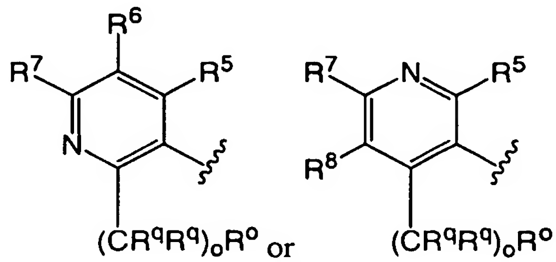
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$,

$-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo,

cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

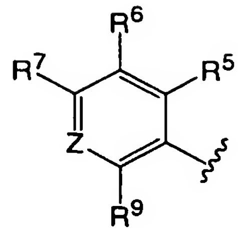
R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

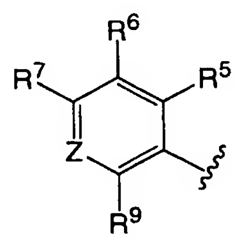
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; or

R^2 is -(C(R^q)$_2$)$_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and -N$R^m$$C_{2-6}$alkylO$R^m$; or

R^2 is -(C(R^q)$_2$)$_o$$R^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S,

wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected

from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR$^mR^m$, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR$^mR^m$, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR$^mR^s$, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR$^mR^s$, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR$^mR^m$, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR$^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR$^mR^s$, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR$^mR^s$, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

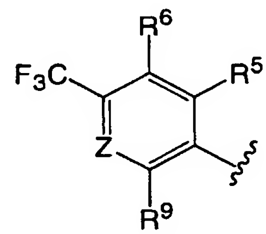
R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{m}R^m, -O-C$_{1-6}$alkylOR^m, -NR^{m}R^m, -NR^m-C$_{1-4}$haloalkyl, -NR^m-C$_{1-6}$alkylNR^{m}R^m or -NR^m-C$_{1-6}$alkylOR^m;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, -OR^m, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^n, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -NR^{m}C$_{2-6}$alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m,

$-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

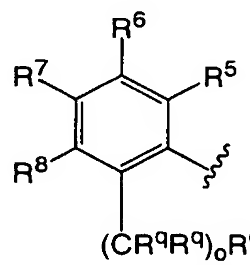
R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

81. A compound according to Claim 80, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge

are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

82. A compound according to Claim 81, wherein:

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$,

$-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

83. A compound according to Claim 81, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

84. A compound according to Claim 81, wherein R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-NR^mR^m$ or $-NR^m-C_{1-4}haloalkyl$.

85. A compound according to Claim 81, wherein R^7 is $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, I, Br or Cl.

86. A compound according to Claim 81, wherein R^7 is tert-butyl or trifluoromethyl.

87. A compound according to Claim 81, wherein R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

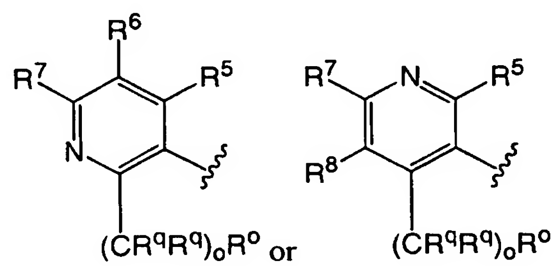
88. A compound according to Claim 81, wherein R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

89. A compound according to Claim 81, wherein Y is O.

90. A compound according to Claim 81, wherein Y is NH.

91. A compound according to Claim 80, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl,

C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and -N$R^m$$C_{2-6}$alkylO$R^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m; [C_{1-8}alkyl, C_{1-5}haloalkyl, I, Br or Cl]

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

92. A compound according to Claim 91, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$,

$-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

93. A compound according to Claim 91, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

94. A compound according to Claim 91, wherein R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-NR^mR^m$ or $-NR^m-C_{1-4}haloalkyl$.

95. A compound according to Claim 91, wherein R^7 is $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, I, Br or Cl.

96. A compound according to Claim 91, wherein R^7 is tert-butyl or trifluoromethyl.

97. A compound according to Claim 91, wherein R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

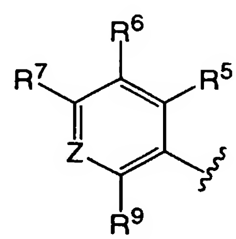
98. A compound according to Claim 91, wherein R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

99. A compound according to Claim 91, wherein Y is O.

100. A compound according to Claim 91, wherein Y is NH.

101. A compound according to Claim 80, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl,

halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

201. A compound according to Claim 101, wherein R^4 is a heterocycle selected from indole, 3H-indole, benzo[b]furan, benzothiophene, 1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 1,2,3,4-tetrahydroquinoline, isoquinoline, cinnoline, phthalazine, quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

103. A compound according to Claim 101, wherein R^4 is a heterocycle selected from 6-indole, 7-indole, 6-3H-indole, 7-3H-indole, 6-benzo[b]furan, 7-benzo[b]furan, 6-benzothiophene, 7-benzothiophene, 6-1H-indazole, 7-1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 7-1,2,3,4-tetrahydroquinoline, 8-1,2,3,4-tetrahydroquinoline, isoquinolin-7-yl, isoquinolin-8-yl, 7-cinnoline, 8-cinnoline, phthalazine, 7-quinazoline, 8-quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

104. A compound according to Claim 101, wherein R^9 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^{m}R^m, -O-C_{1-6}alkylOR^m, -NR^{m}R^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^{m}R^m or -NR^m-C_{1-6}alkylOR^m.

105. A compound according to Claim 101, wherein R^9 is H.

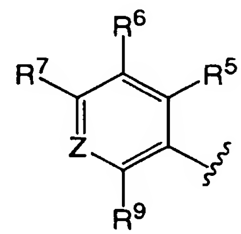
106. A compound according to Claim 101, wherein Z is CR^8.

107. A compound according to Claim 101, wherein Z is N.

~~108. A compound according to Claim 101, wherein R^7 is tert-butyl or~~ trifluoromethyl.

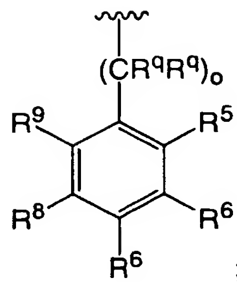
109. A compound according to Claim 80, wherein:

R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC_{2-6}alkylNR^{m}R^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^mC_{2-6}alkylNR^{m}R^m and -NR^mC_{2-6}alkylOR^m; or

R^2 is



; or

R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$,

$-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

110. A compound according to Claim 109, wherein R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

111. A compound according to Claim 109, wherein R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

112. A compound according to Claim 109, wherein R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$,

$-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

113. A compound according to Claim 109, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

114. A compound according to Claim 109, wherein R^7 is tert-butyl or trifluoromethyl.

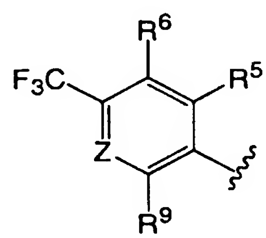
115. A compound according to Claim 109, wherein R^9 is H.

116. A compound according to Claim 109, wherein Z is CR^8.

117. A compound according to Claim 109, wherein Z is N.

118. A compound according to Claim 80, wherein:

R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$,

$-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

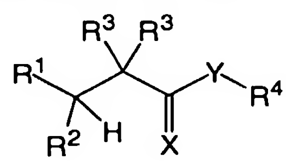
119. A compound according to Claim 118, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$,

$-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

~~120. A compound according to Claim 118, wherein Z is CR^8.~~

121. A compound according to Claim 118, wherein Z is N.

122. A compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance $C_{1-8}alkyl$, phenyl or benzyl;

R^q is independently in each instance H, $C_{1-4}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

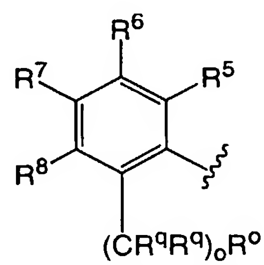
R^3 is H or C_{1-4}alkyl;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$,

$-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

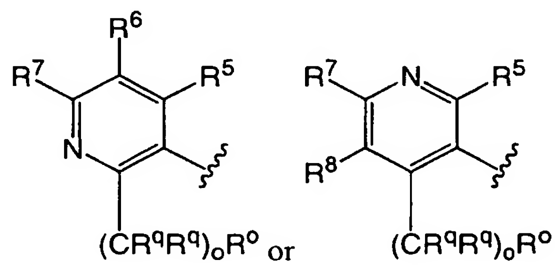
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or

2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$,

$-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

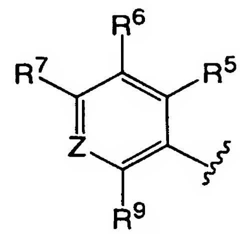
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

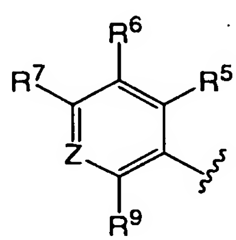
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from

C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$,

$-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

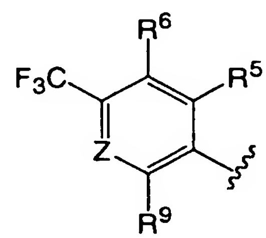
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$,

$-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

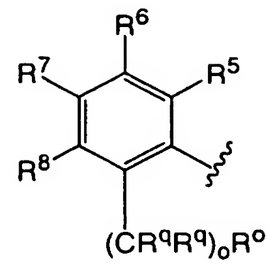
R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

123. A compound according to Claim 122, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

124. A compound according to Claim 123, wherein:

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O

and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m , $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

125. A compound according to Claim 123, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$,

$-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

126. A compound according to Claim 123, wherein R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-NR^mR^m$ or $-NR^m-C_{1-4}$haloalkyl.

127. A compound according to Claim 123, wherein R^7 is C_{1-5}alkyl, C_{1-4}haloalkyl, I, Br or Cl.

127. A compound according to Claim 123, wherein R^7 is tert-butyl or trifluoromethyl.

129. A compound according to Claim 123, wherein R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

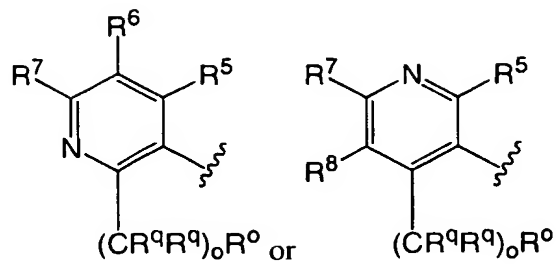
130. A compound according to Claim 123, wherein R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

131. A compound according to Claim 123, wherein Y is O.

132. A compound according to Claim 123, wherein Y is NH.

133. A compound according to Claim 122, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$,

$-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; [C_{1-8}alkyl, C_{1-5}haloalkyl, I, Br or Cl]

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH.

134. A compound according to Claim 133, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms

being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m , $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

135. A compound according to Claim 133, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$,

$-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

136. A compound according to Claim 133, wherein R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-NR^mR^m$ or $-NR^m-C_{1-4}haloalkyl$.

137. A compound according to Claim 133, wherein R^7 is $C_{1-5}alkyl$, $C_{1-4}haloalkyl$, I, Br or Cl.

138. A compound according to Claim 133, wherein R^7 is tert-butyl or trifluoromethyl.

139. A compound according to Claim 133, wherein R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic ring containing 0, 1, 2 or 3 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 1, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

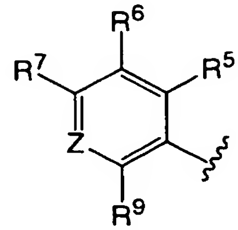
140. A compound according to Claim 133, wherein R^o is a saturated, partially-saturated or unsaturated 6-membered ring containing 0, 1, 2 or 3 N atoms, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p.

141. A compound according to Claim 133, wherein Y is O.

142. A compound according to Claim 133, wherein Y is NH.

143. A compound according to Claim 122, wherein:

R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$,

$-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

144. A compound according to Claim 143, wherein R^4 is a heterocycle selected from indole, 3H-indole, benzo[b]furan, benzothiophene, 1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 1,2,3,4-tetrahydroquinoline, isoquinoline, cinnoline, phthalazine, quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-9}alkyl$, oxo, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$,

-SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m , -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and -NR^{m}C$_{2-6}$alkylOR^m.

145. A compound according to Claim 143, wherein R^4 is a heterocycle selected from 6-indole, 7-indole, 6-3H-indole, 7-3H-indole, 6-benzo[b]furan, 7-benzo[b]furan, 6-benzothiophene, 7-benzothiophene, 6-1H-indazole, 7-1H-indazole, benzimidazole, benzthiazole, 1H-benzotriazole, 7-quinoline, 8-quinoline, 7-1,2,3,4-tetrahydroquinoline, 8-1,2,3,4-tetrahydroquinoline, isoquinolin-7-yl, isoquinolin-8-yl, 7-cinnoline, 8-cinnoline, phthalazine, 7-quinazoline, 8-quinazoline and quinoxaline, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C$_{1-9}$alkyl, oxo, C$_{1-4}$haloalkyl, halo, nitro, cyano, -OR^m, -S(=O)$_n$C$_{1-6}$alkyl, -O-C$_{1-4}$haloalkyl, -O-C$_{1-6}$alkylNR^{m}R^m, -O-C$_{1-6}$alkylOR^m, -NR^{m}R^m, -NR^m-C$_{1-4}$haloalkyl, -NR^m-C$_{1-6}$alkylNR^{m}R^m, -NR^m-C$_{1-6}$alkylOR^m, -C(=O)C$_{1-6}$alkyl, -OC(=O)C$_{1-6}$alkyl, -C(=O)NR^{m}C$_{1-6}$alkyl, -NR^{m}C(=O)C$_{1-6}$alkyl -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C$_{1-4}$alkyl substituted by 1 or 2 groups selected from C$_{1-2}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m,

$-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

146. A compound according to Claim 143, wherein R^9 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$.

147. A compound according to Claim 143, wherein R^9 is H.

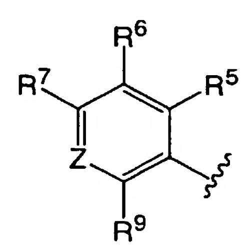
148. A compound according to Claim 143, wherein Z is CR^8.

149. A compound according to Claim 143, wherein Z is N.

150. A compound according to Claim 101, wherein R^7 is tert-butyl or trifluoromethyl.

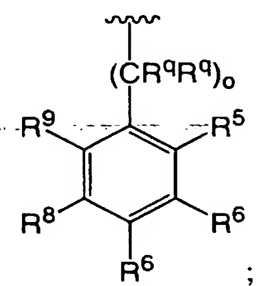
151. A compound according to Claim 122, wherein:

R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is



; or

R^2 is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^5, R^6 and R^7;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$,

$-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

152. A compound according to Claim 151, wherein R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from $C_{1-4}haloalkyl$, halo, cyano,

nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

153. A compound according to Claim 151, wherein R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$,

$-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$.

154. A compound according to Claim 151, wherein R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

155. A compound according to Claim 151, wherein R^4 is a phenyl ring that is vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$,

$-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$; and the bridge carbon atoms are substituted with 0, 1 or 2 =O groups.

156. A compound according to Claim 151, wherein R^7 is tert-butyl or trifluoromethyl.

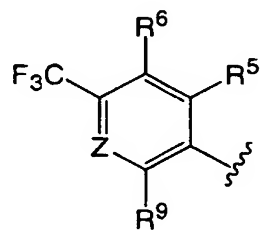
157. A compound according to Claim 151, wherein R^9 is H.

158. A compound according to Claim 151, wherein Z is CR^8.

159. A compound according to Claim 151, wherein Z is N.

160. A compound according to Claim 122, wherein:

R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$,

-N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$, -N$R^m$$C_{2-6}$alkylO$R^m$, -C(=O)$R^s$, -C(=O)O$R^s$, -C(=O)N$R^mR^s$, -C(=N$R^m$)N$R^mR^s$, -O$R^s$, -OC(=O)$R^s$, -OC(=O)N$R^mR^s$, -OC(=O)N($R^m$)S(=O)$_2R^s$, -O$C_{2-6}$alkylN$R^mR^s$, -O$C_{2-6}$alkylO$R^s$, -S$R^s$, -S(=O)$R^s$, -S(=O)$_2R^s$, -S(=O)$_2NR^mR^s$, -S(=O)$_2$N($R^m$)C(=O)$R^s$, -S(=O)$_2$N($R^m$)C(=O)O$R^s$, -S(=O)$_2$N($R^m$)C(=O)N$R^mR^s$, -N$R^mR^s$, -N($R^m$)C(=O)$R^s$, -N($R^m$)C(=O)O$R^s$, -N($R^m$)C(=O)N$R^mR^s$, -N($R^m$)C(=N$R^m$)N$R^mR^s$, -N($R^m$)S(=O)$_2R^s$, -N($R^m$)S(=O)$_2NR^mR^s$, -N$R^m$$C_{2-6}$alkylN$R^mR^s$, -N$R^m$$C_{2-6}$alkylO$R^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylNR^mR^m, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m, -N(R^m)C(=NR^m)NR^mR^m, -N(R^m)S(=O)$_2R^n$, -N(R^m)S(=O)$_2$NR^mR^m, -N$R^m$$C_{2-6}$alkylN$R^mR^m$ and -N$R^m$$C_{2-6}$alkylO$R^m$; wherein R^4 is not unsubstituted phenyl;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, -OC_{1-6}alkyl, -O-C_{1-4}haloalkyl, -O-C_{1-6}alkylNR^mR^m, -O-C_{1-6}alkylOR^m, -NR^mR^m, -NR^m-C_{1-4}haloalkyl, -NR^m-C_{1-6}alkylNR^mR^m or -NR^m-C_{1-6}alkylOR^m;

Y is NH; and

Z is CR^8 or N.

161. A compound according to Claim 160, wherein R^4 is a saturated or unsaturated 5- or 6-membered ring containing 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, -C(=O)NR^mR^m, -C(=NR^m)NR^mR^m, -OR^n, -OC(=O)R^n, -OC(=O)NR^mR^m, -OC(=O)N(R^m)S(=O)$_2R^n$, -OC_{2-6}alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2R^n$, -S(=O)$_2$NR^mR^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^mR^m, -NR^mR^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^mR^m,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ and $-NR^mC_{2-6}alkylOR^m$;

162. A compound according to Claim 160, wherein Z is CR^8.

163. A compound according to Claim 160, wherein Z is N.

164. A compound according to Claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compounds is selected from:
(2E)-3-[4-(tert-butyl)phenyl]-N-phenylprop-2-enamide,
(2E)-N-(3,4-dimethoxyphenyl)-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(4-hydroxy-3-methoxyphenyl)prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(2-5,6,7,8-tetrahydronaphthyl)prop-2-enamide,
(2E)-N-(2H,3H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(3-oxo(2H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide,

(2E)-3-[4-(tert-butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(4-methyl(2H,3H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(3-oxo(2H,4H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide,
(2E)-N-(2H,3H,4H-benzo[e]1,4-oxazaperhydroin-7-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(4-methyl-3-oxo(2H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(4-methyl(2H,3H-benzo[e]1,4-oxazaperhydroin-7-yl))prop-2-enamide,
ethyl 6-{(2E)-3-[4-(tert-butyl)phenyl]prop-2-enoylamino}-2H,3H,4H-benzo[e]1,4-oxazaperhydroine-2-carboxylate,
(2E)-3-[4-(tert-butyl)phenyl]-N-[2-(hydroxymethyl)(2H,3H,4H-benzo[3,4-e]1,4-oxazaperhydroin-6-yl)]prop-2-enamide,
(2E)-N-[(3S)-3-(hydroxymethyl)(2H,3H-benzo[e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-[(3R)-3-(hydroxymethyl)(2H,3H-benzo[e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-[(2R)-2-(hydroxymethyl)(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-[(2S)-2-(hydroxymethyl)(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)]-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(7-1,2,3,4-tetrahydroquinolyl)prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1-methyl(7-1,2,3,4-tetrahydroquinolyl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(2-oxo(6-1,3,4-trihydroquinolyl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(2-oxo(7-1,3,4-trihydroquinolyl))prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(3-hydroxyphenyl)prop-2-enamide,
2-(3-{(2E)-3-[4-(tert-butyl)phenyl]prop-2-enoylamino}phenoxy)acetic acid,
(2E)-3-[4-(tert-butyl)phenyl]-N-[3-(2-hydroxyethoxy)phenyl]prop-2-enamide,

(2E)-3-[4-(tert-butyl)phenyl]-N-[3-(2-methoxyethoxy)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-{3-[2-(1,3-dioxobenzo[c]azolin-2-yl)ethoxy]phenyl}prop-2-enamide,
(2E)-N-[3-(2-Aminoethoxy)phenyl]-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-indolin-6-ylprop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1-methylindolin-6-yl)prop-2-enamide,
(2E)-N-(1-Acetyl-3,3-dimethylindolin-6-yl)-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1,3,3-trimethylindolin-6-yl)prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1-methylindol-6-yl)prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1-methylindol-5-yl)prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(1-methylindolin-5-yl)prop-2-enamide,
(2E)-N-benzoxazol-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-benzoxazol-6-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-benzo[b]furan-5-yl-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-(2,3-dihydrobenzo[b]furan-5-yl)prop-2-enamide,
N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3,3-bis(4-methylphenyl)prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-methylprop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-2-ethylprop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-(4-cyclopropylphenyl)prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)(3-pyridyl)]prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[3-(tert-butyl)phenyl]prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[2-fluoro-4-(trifluoromethyl)-phenyl]prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[2,3-difluoro-4-(trifluoromethyl)-phenyl]prop-2-enamide,

(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[2,4-bis(trifluoromethyl)-phenyl]prop-2-enamide,

(2E)-3-[2-fluoro-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide,

(2E)-3-[2,3-difluoro-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide,

(2E)-3-[2,4-bis(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide,

N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide,

(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-phenylbut-2-enamide,

(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-5-methylhex-2-enamide,

N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-iodoprop-2-enamide,

(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-(3-aminophenyl)-3-[4-(tert-butyl)phenyl]prop-2-enamide,

ethyl (4E)-5-(N-(2H,3H-benzo[e]1,4-dioxan-6-yl)carbamoyl)-4-[4-(tert-butyl)phenyl]pent-4-enoate,

3-methoxyphenyl (2E)-3-[4-(tert-butyl)phenyl]prop-2-enoate,

N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-hydroxyprop-2-enamide,

N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)[7-(tert-butyl)(3-isoquinolyl)]-carboxamide,

N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]prop-2-enamide,

N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-3-phenylprop-2-enamide,

(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-3-phenylprop-2-enamide,

(2E)-3-[4-(tert-butyl)phenyl]-N-[1-(N-methylcarbamoyl)(1H-indazol-6-yl)]prop-2-enamide,

(2E)-3-[4-(tert-butyl)phenyl]-N-{4-chloro-3-[(methylamino)carbonylamino]-phenyl}prop-2-enamide,

(2E)-3-[4-(tert-butyl)phenyl]-N-quinoxalin-6-ylprop-2-enamide,
(2E)-N-(1-acetyl(7-1,2,3,4-tetrahydroquinolyl))-3-[4-(tert-butyl)phenyl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[1-(2-methoxyethyl)indol-6-yl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[1-(2-methoxyethyl)indol-5-yl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-6-yl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]prop-2-enamide,
(2E)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]-N-indol-6-ylprop-2-enamide,
(2E)-N-benzothiazol-6-yl-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]prop-2-enamide,
(2E)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]-N-indol-5-ylprop-2-enamide,
(2E)-3-[6-(tert-butyl)-2-methyl(3-pyridyl)]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide,
(2E)-3-[6-(tert-butyl)(3-pyridyl)]-N-[2-(hydroxymethyl)indol-5-yl]prop-2-enamide,
(2E)-3-[6-(tert-butyl)(3-pyridyl)]-N-[1-(2-hydroxyethyl)indol-5-yl]prop-2-enamide,
(2E)-N-indol-6-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide,
(2E)-N-indol-5-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide,
(2E)-N-benzothiazol-6-yl-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide,
(2E)-N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[2-methyl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide,
(2E)-3-[4-(tert-butyl)phenyl]-N-[3-(hydroxymethyl)-2-oxo(7-1,3,4-trihydroquinolyl)]prop-2-enamide,
(2E)-N-[3-(hydroxymethyl)(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-N-[3-(hydroxymethyl)-1-methyl(7-1,2,3,4-tetrahydroquinolyl)]-3-[4-(trifluoromethyl)phenyl]prop-2-enamide,

(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-5-(1,3-dioxolan-2-yl)pent-2-enamide,
(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-4-(3-pyridyl)but-2-enamide,
N-(2H,3H-benzo[e]1,4-dioxan-6-yl)(2Z)-3-[4-(tert-butyl)phenyl]-4-pyrrolidinylbut-2-enamide,
(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]-6-imidazolylhex-2-enamide,
3-(4-tert-butyl-phenyl)-6-imidazol-1-yl-hex-2-enoic acid benzothiazol-6-ylamide,
(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[2-morpholin-4-yl-6-(trifluoromethyl)(3-pyridyl)]prop-2-enamide,
(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)-2-bromophenyl]prop-2-enamide,
ethyl 2-[(1E)-2-(N-(2H,3H-benzo[e]1,4-dioxan-6-yl)carbamoyl)vinyl]-5-(tert-butyl)benzoate,
(2E)-3-[2-Bromo-4-(trifluoromethyl)phenyl]-N-indol-5-ylprop-2-enamide,
(2E)-N-benzothiazol-6-yl-3-[2-bromo-4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-N-(2H,3H-benzo[e]1,4-dioxan-6-yl)-3-[2-bromo-4-(trifluoromethyl)-phenyl]prop-2-enamide,
(2E)-N-indol-5-yl-3-[2-(6-methoxy(3-pyridyl))-4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-N-indol-5-yl-3-[2-(4-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-N-indol-5-yl-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide,
tert-butyl 4-{2-[(1E)-2-(N-indol-5-ylcarbamoyl)vinyl]-5-(trifluoromethyl)phenyl}-1,2,5,6-tetrahydropyridinecarboxylate,
(2E)-N-indol-5-yl-3-[2-(1,3-thiazol-2-yl)-4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-N-indol-5-yl-3-[2-(3-pyridylmethyl)-4-(trifluoromethyl)phenyl]prop-2-enamide,
(2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]-N-(7-quinolyl)prop-2-enamide,
(2E)-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]-N-(3-quinolyl)prop-2-enamide,

(2E)-N-indol-6-yl-3-[2-(3-pyridyl)-4-(trifluoromethyl)phenyl]prop-2-enamide, and

N-(2H,3H-benzo[3,4-e]1,4-dioxan-6-yl)-3-[4-(tert-butyl)phenyl]propanamide.

165. A compound according to Claim 21, or a pharmaceutically-acceptable salt thereof, wherein the compounds is selected from:

(4-benzo[1,3]dioxol-5-yl-pyridin-2-yl)-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine,

(2,3-dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-dimethylamino-phenyl)-pyridin-2-yl]-amine,

(2,3-dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-fluoro-phenyl)-pyridin-2-yl]-amine,

(2,3-dihydro-benzo[1,4]dioxin-6-yl)-[4-(3-trifluoromethyl-phenyl)-pyridin-2-yl]-amine,

(4-benzo[b]thiophen-2-yl-pyridin-2-yl)-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine,

1-{4-[2-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-pyridin-4-yl]-phenyl}-ethanone,

1-{4-[2-(2,3-dihydro-benzo[1,4]dioxin-6-ylamino)-pyridin-4-yl]-phenyl}-ethanol,

[4-(3,5-bis-trifluoromethyl-phenyl)-pyridin-2-yl]-(2,3-dihydro-benzo[1,4]dioxin-6-yl)-amine,

(2,3-dihydro-benzo[1,4]dioxin-6-yl)-[4-(4-trifluoromethoxy-phenyl)-pyridin-2-yl]-amine, and

quinolin-3-yl- [4-(4-trifluoromethyl-phenyl)-pyridin-2-yl]-amine.

166. A compound according to Claim 56, or a pharmaceutically-acceptable salt thereof, wherein the compounds is selected from:

7-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinoline,

2-(3-methoxy-phenoxy)-4-(4-trifluoromethyl-phenyl)-pyridine,

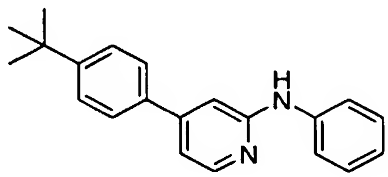
8-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinolin-2-ylamine,

4-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-benzothiazol-2-ylamine,

N-{4-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-benzothiazol-2-yl}-acetamide,

8-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-quinoline, and
2-methyl-5-[4-(4-trifluoromethyl-phenyl)-pyridin-2-yloxy]-benzothiazole.

167. A compound according to Claim 21, or a pharmaceutically-acceptable salt thereof, wherein the compounds is selected from: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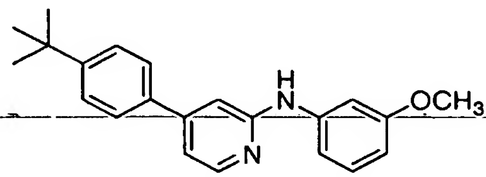
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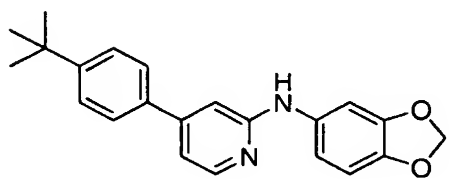
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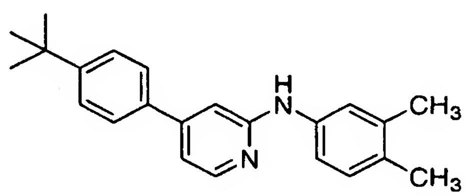
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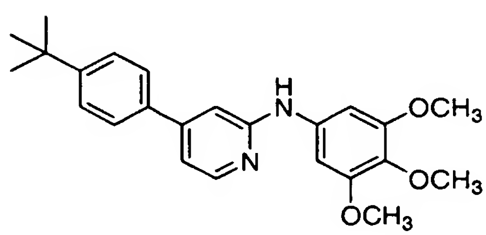
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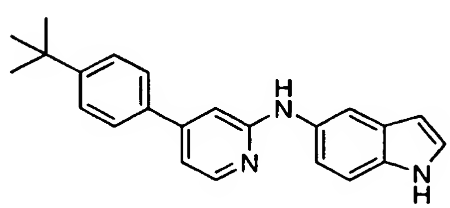
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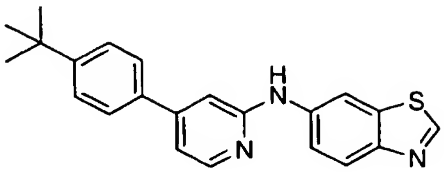
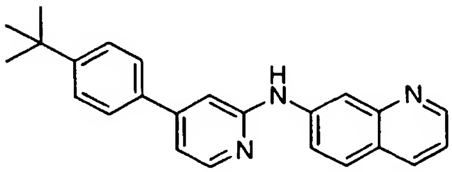
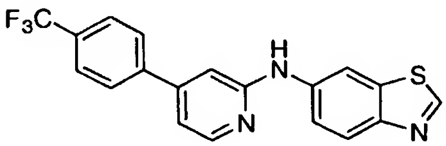
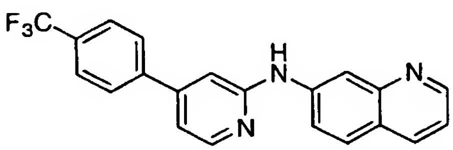
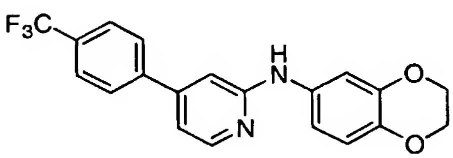
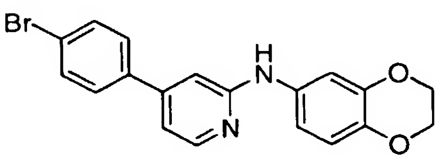
,

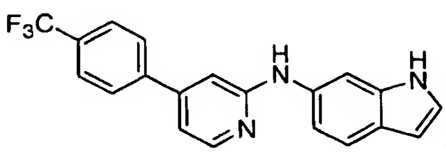
,

,

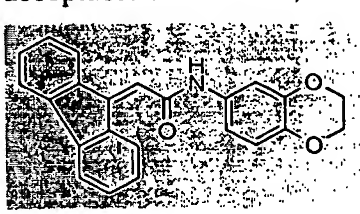
,

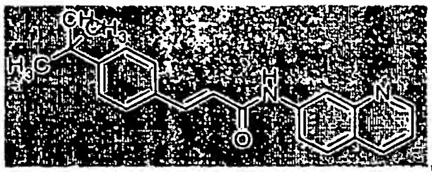
,

, and

.

168. A compound according to Claim 1, or a pharmaceutically-acceptable salt thereof, wherein the compounds is selected from:

,



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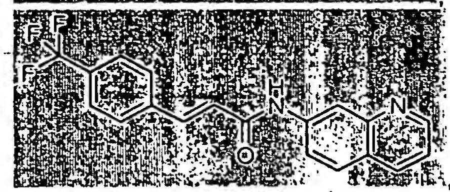

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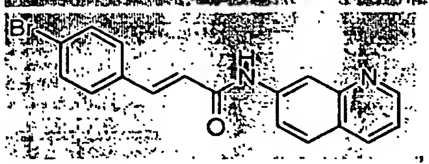

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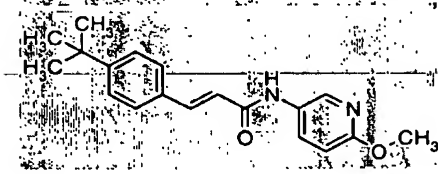

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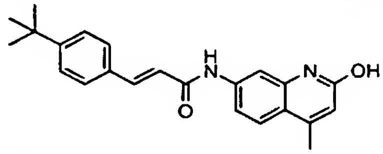

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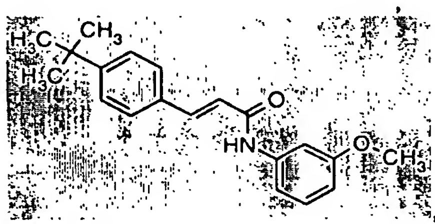

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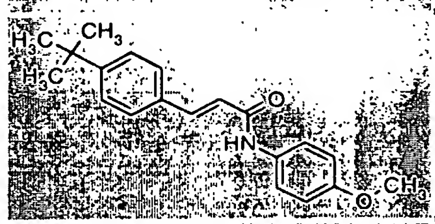

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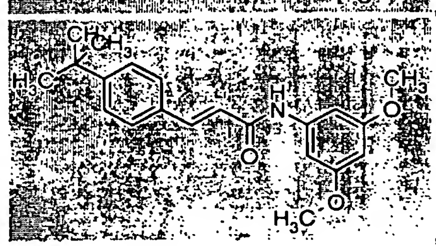

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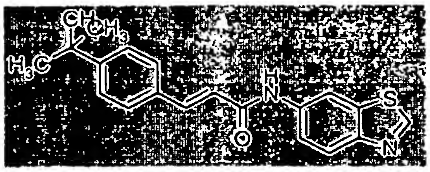
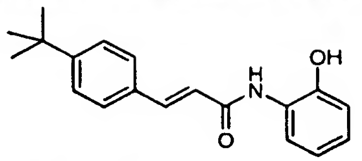
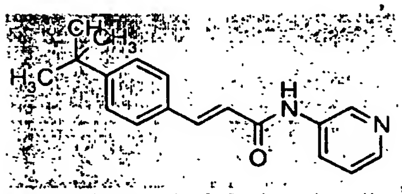
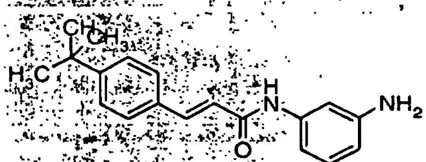
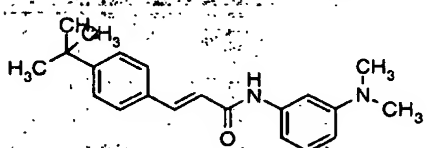
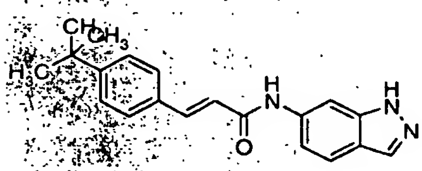
,

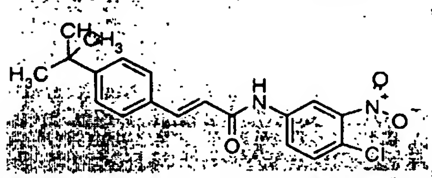
,

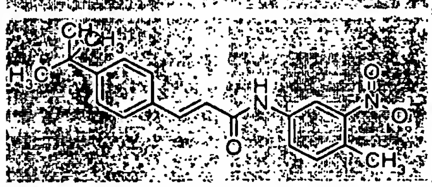
,

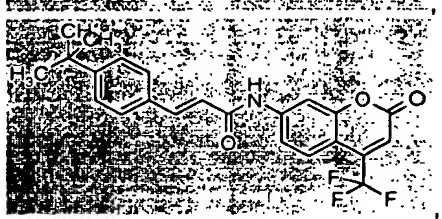
,

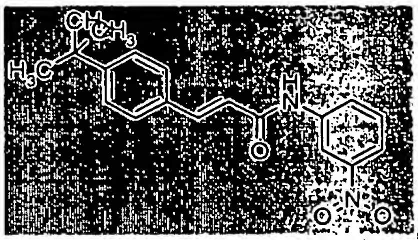
,

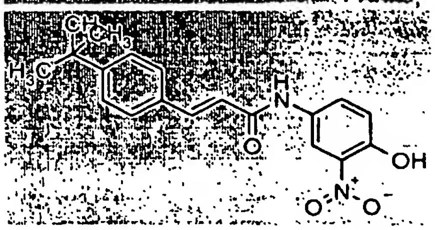
,

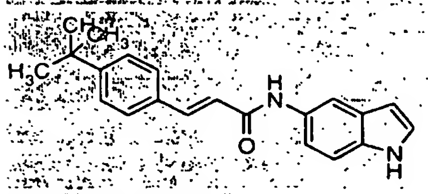
,

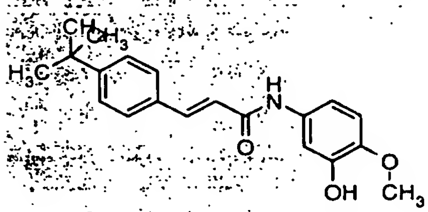
,

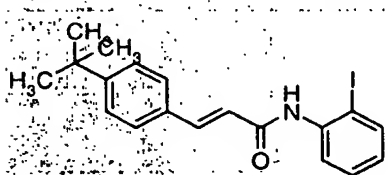
,

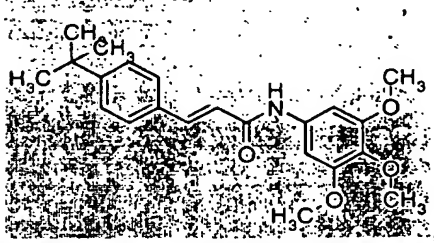
,

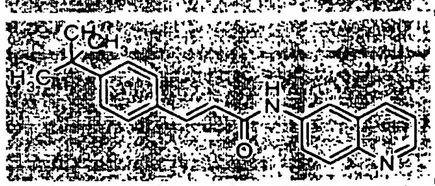
,

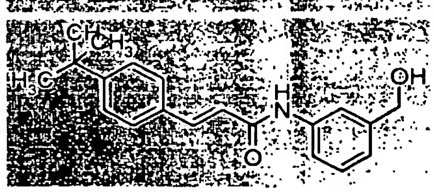
,

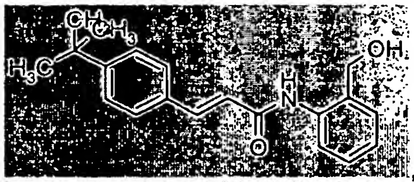
,

,

,

,

,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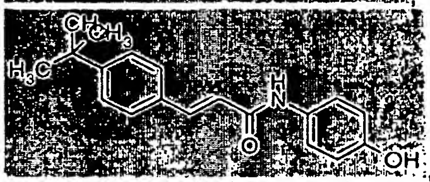
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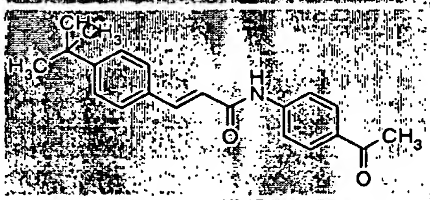
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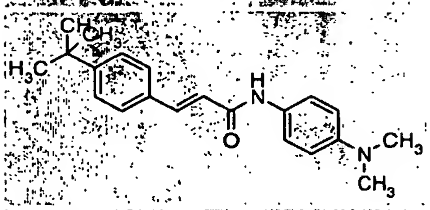
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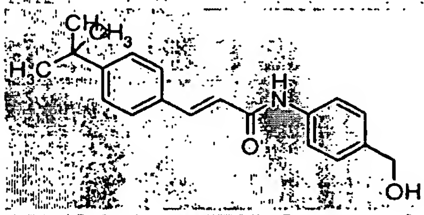
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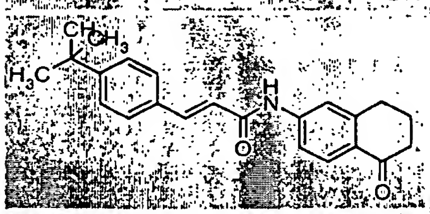
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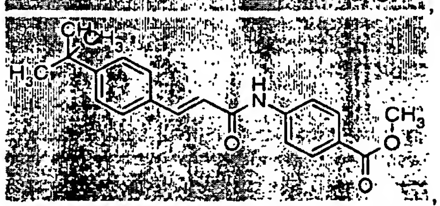
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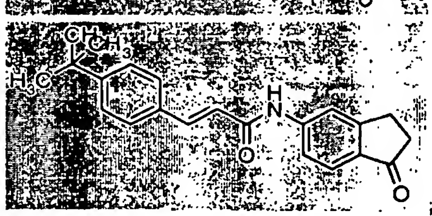
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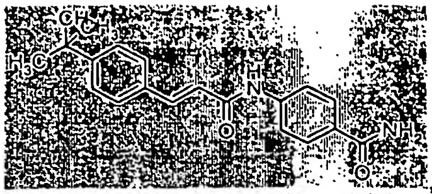
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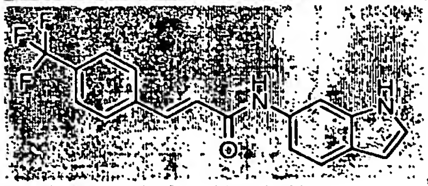
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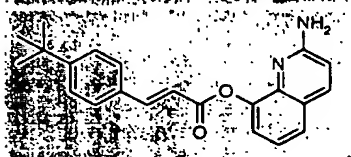
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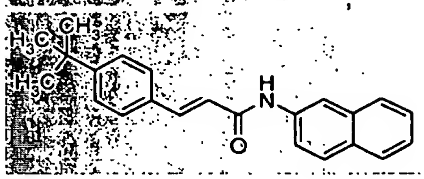
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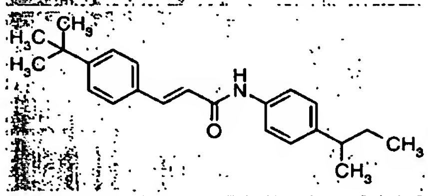
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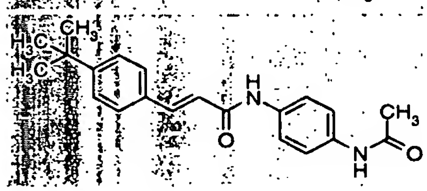
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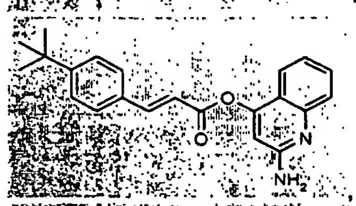
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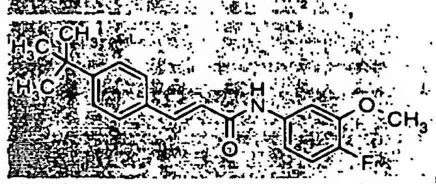
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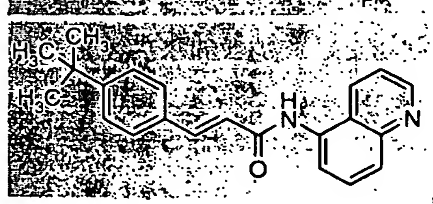
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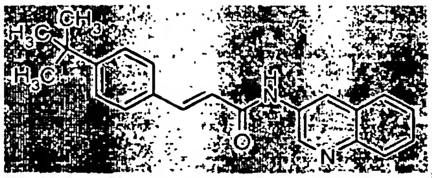
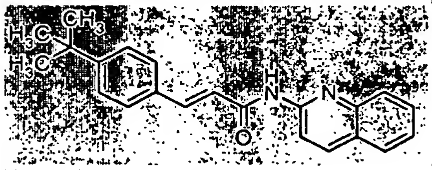
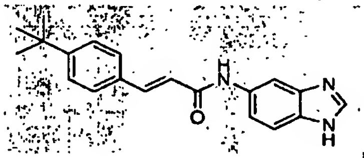
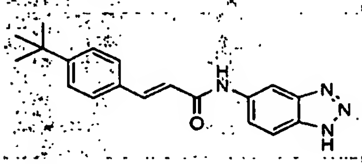
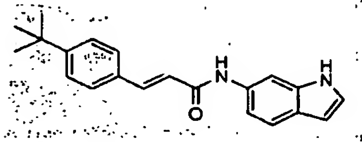
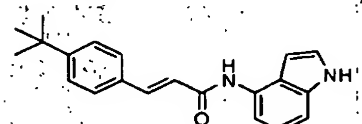
,

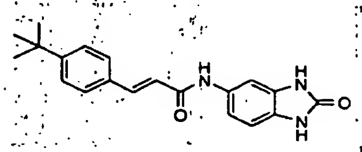
,

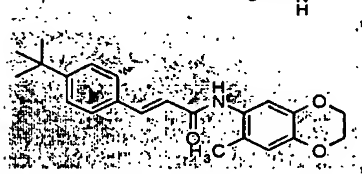
,

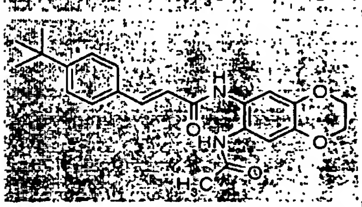
,

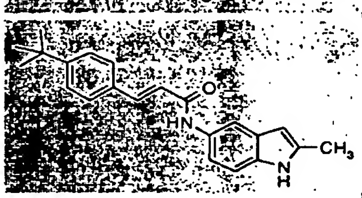
,

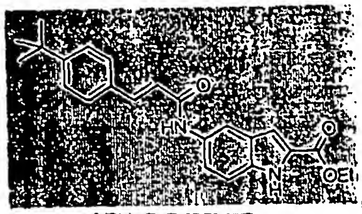
,

,

,

,

,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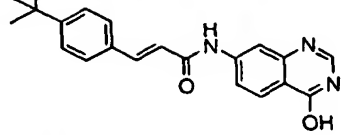
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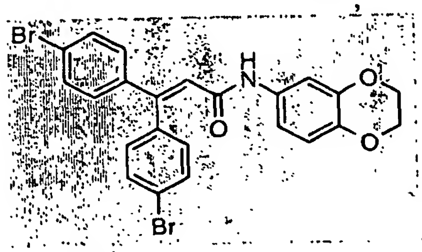
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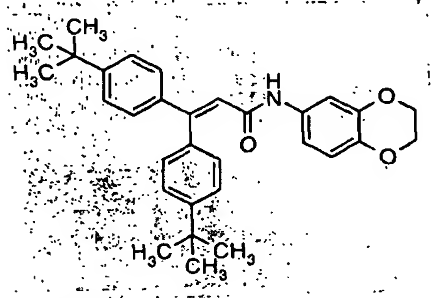
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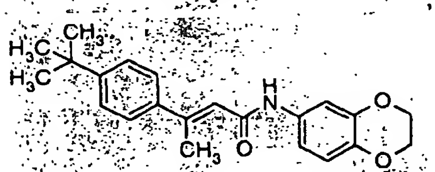
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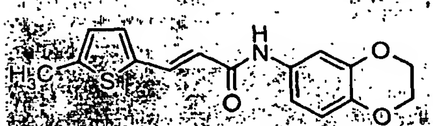
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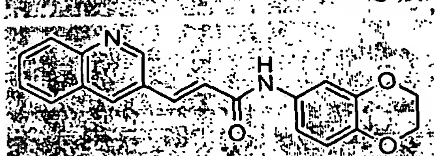
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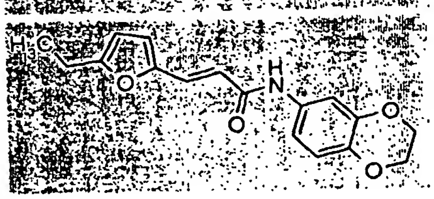
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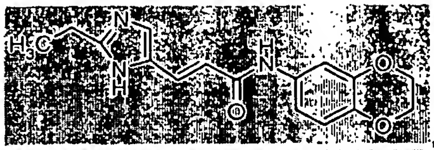
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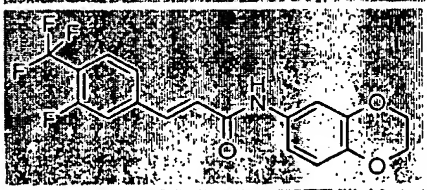
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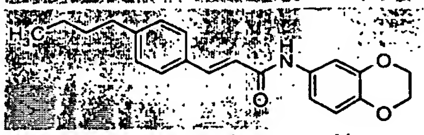
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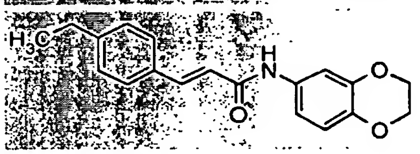
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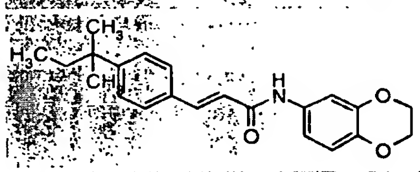
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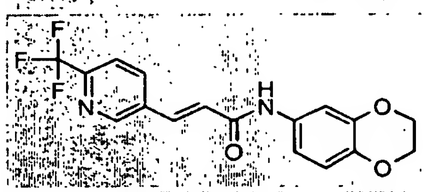
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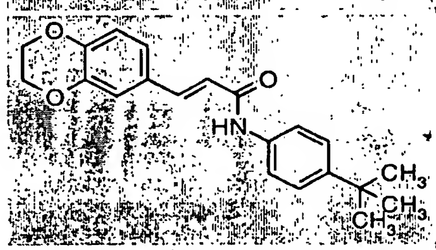
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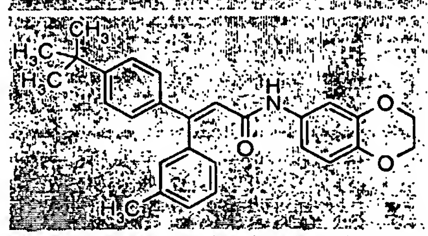
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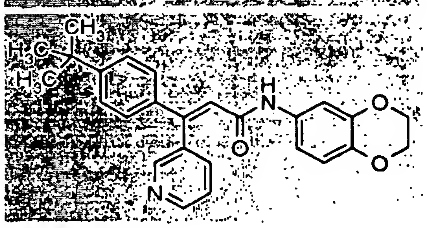
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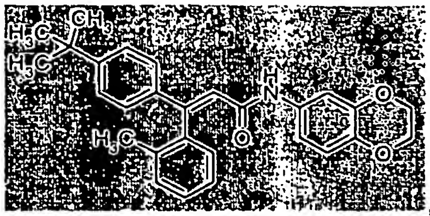
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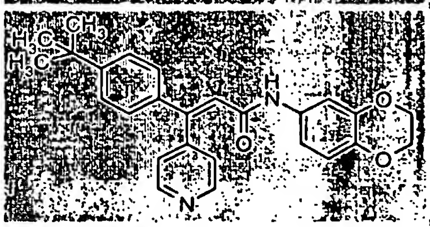
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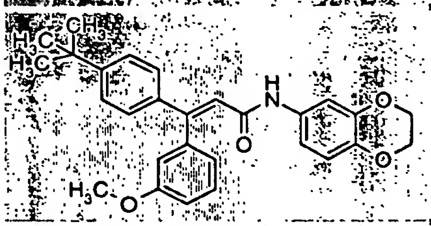
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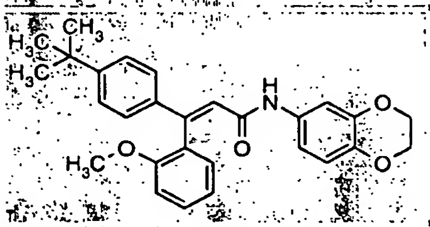
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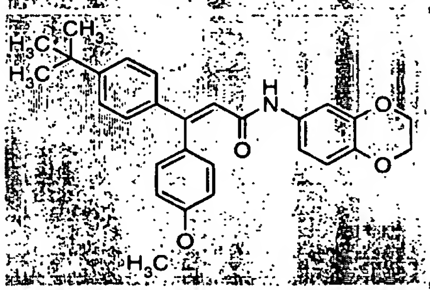
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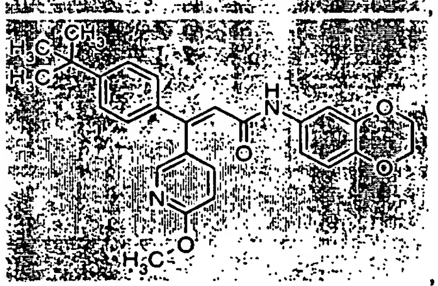
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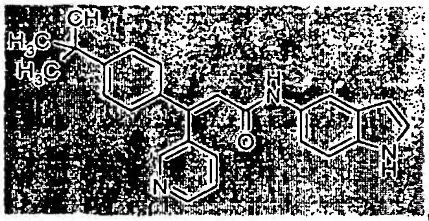
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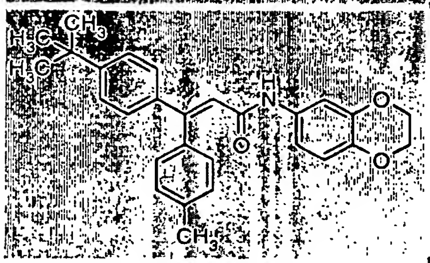
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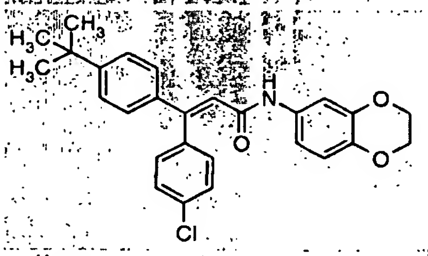
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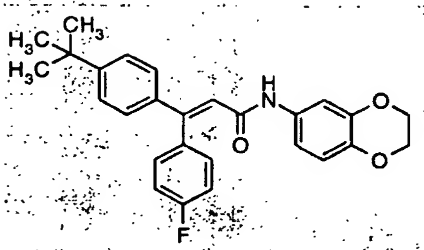
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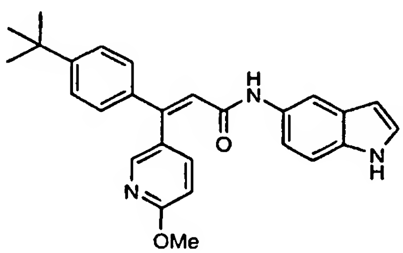
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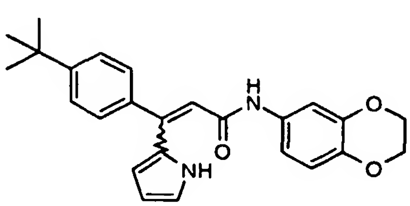
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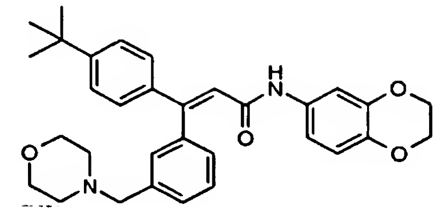

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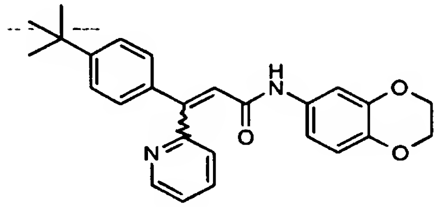

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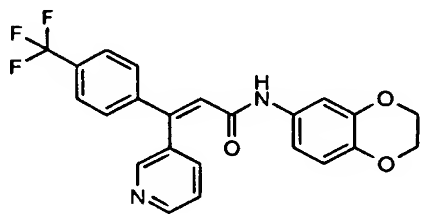

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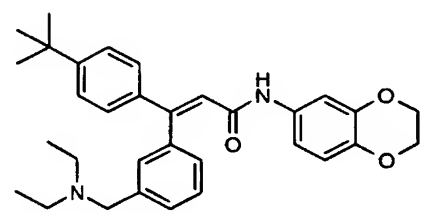

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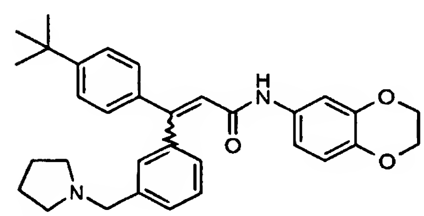

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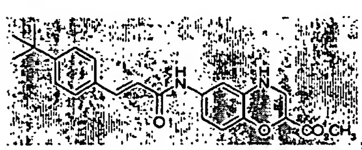

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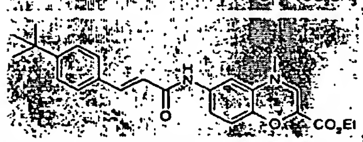

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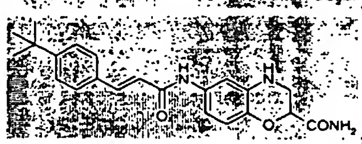

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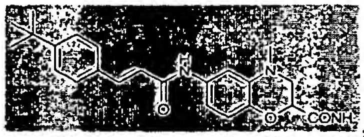
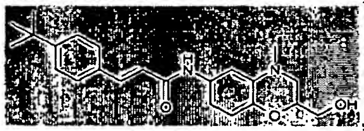
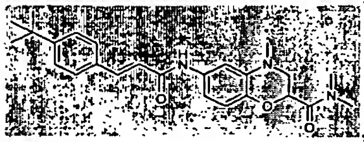
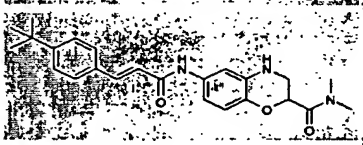
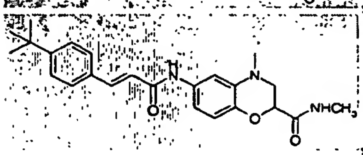
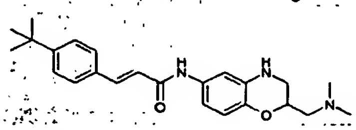
,

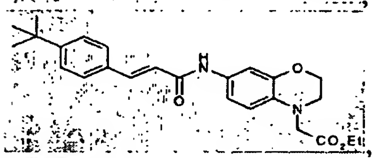
,

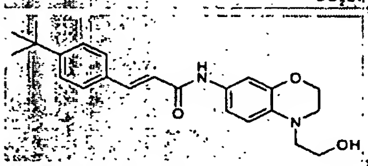
,

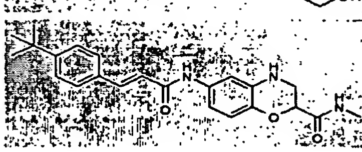
,

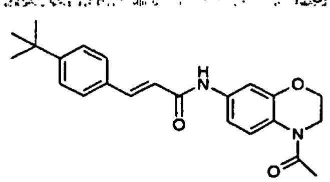
,

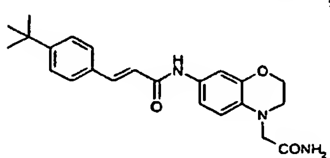
,

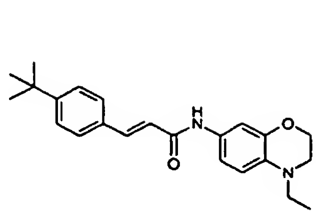
,

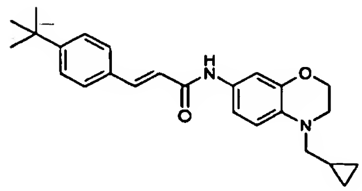
,

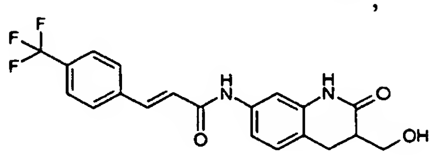
,

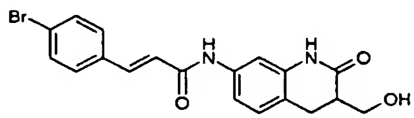
,

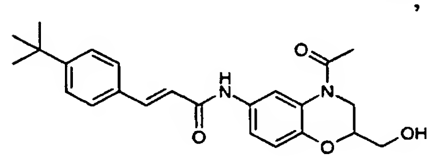
,

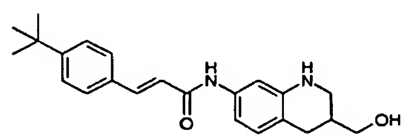
,

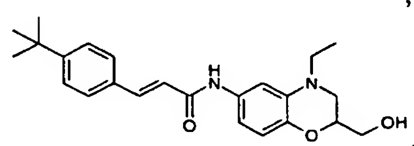
,

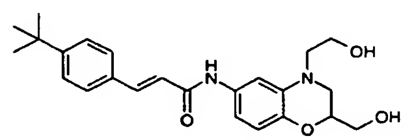
,

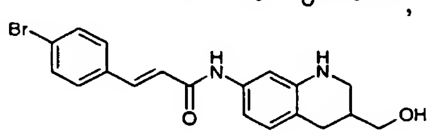
,

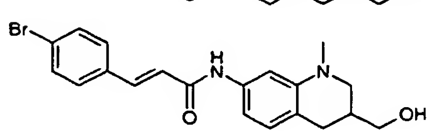
,

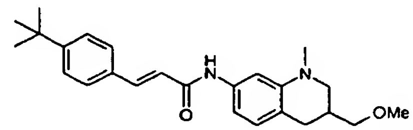
,

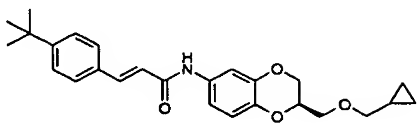
,

,

,

,

,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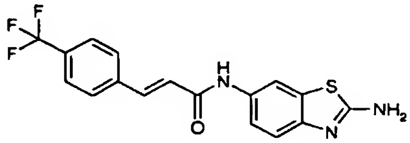
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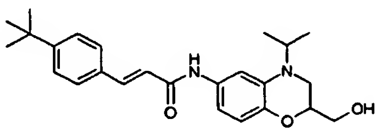
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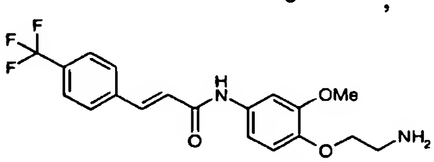
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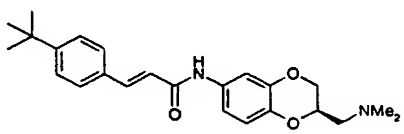
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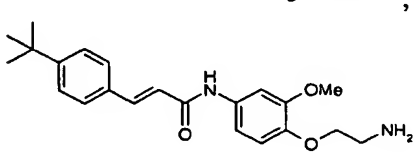
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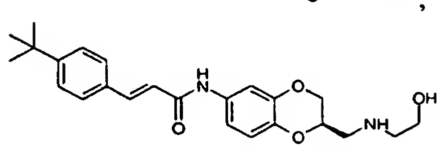
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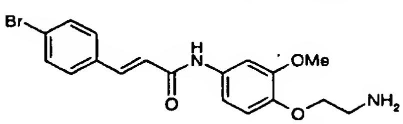
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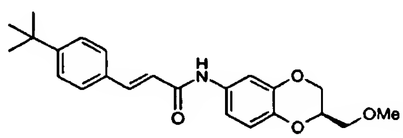
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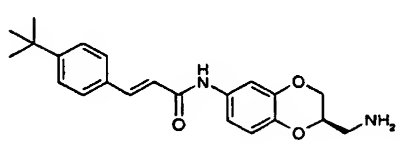
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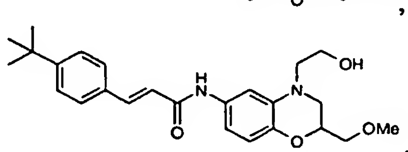
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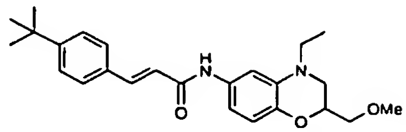
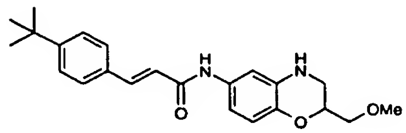
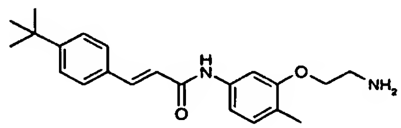
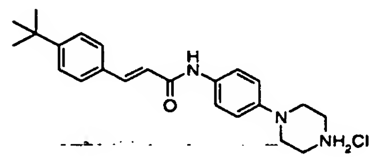
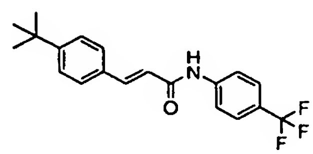
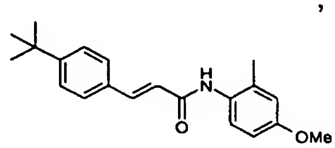
,

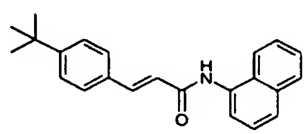
,

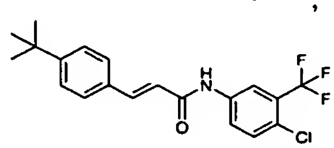
,

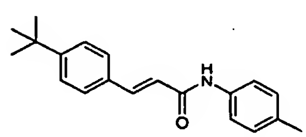
,

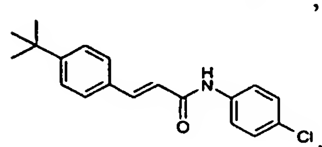
,

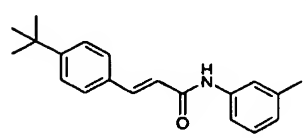
,

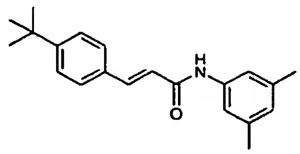
,

,

,

,

,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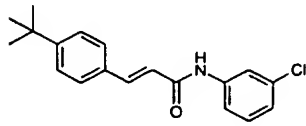
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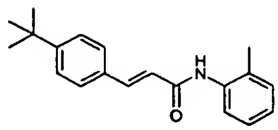
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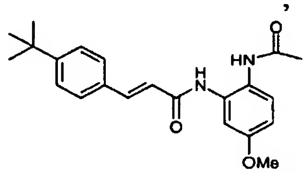
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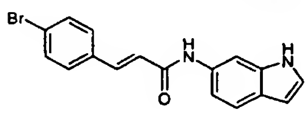
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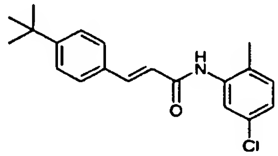
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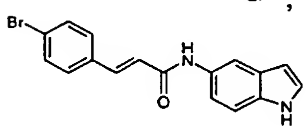
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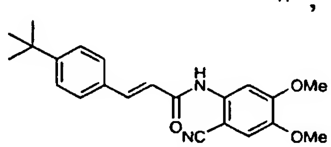
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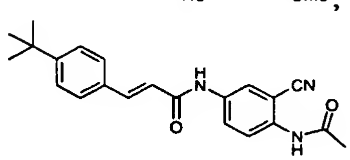
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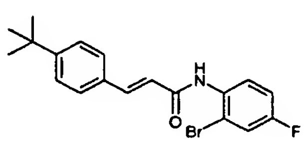
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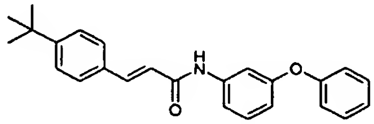
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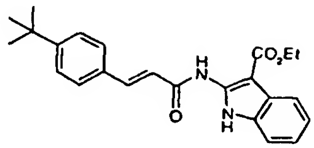
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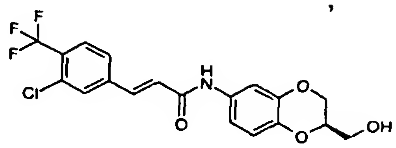
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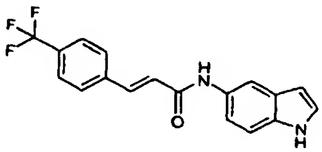
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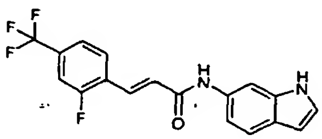
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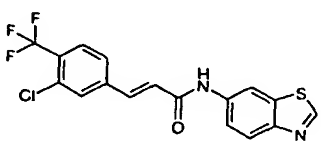
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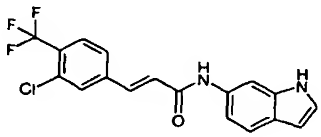
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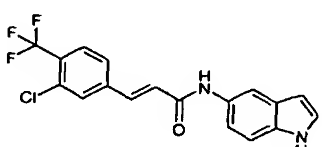
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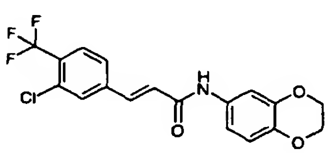
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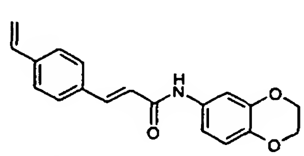
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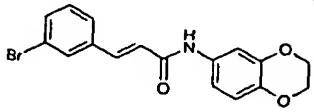
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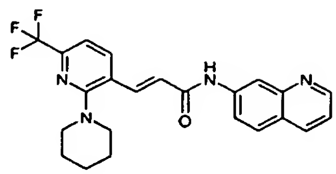
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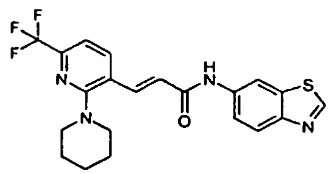
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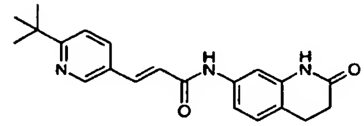
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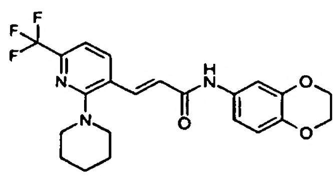
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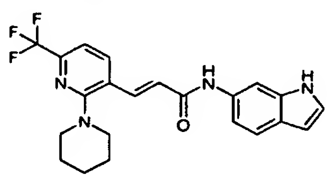
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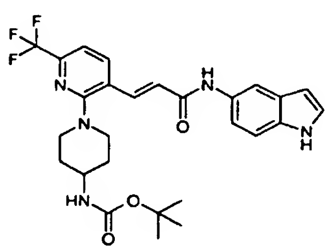
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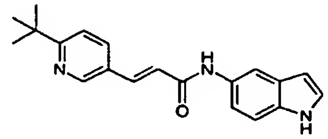
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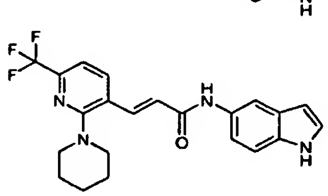
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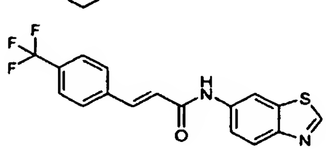
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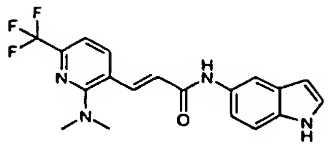
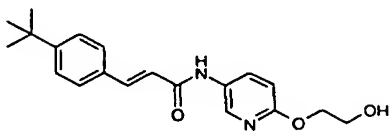
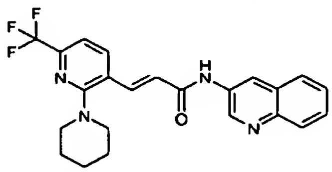
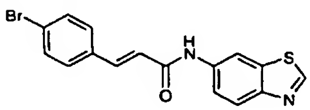
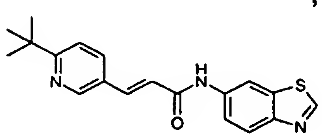
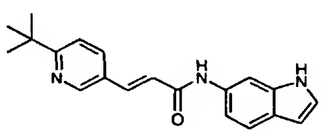
,

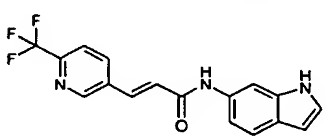
,

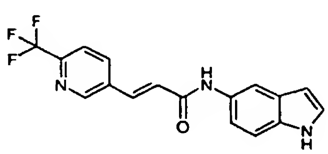
,

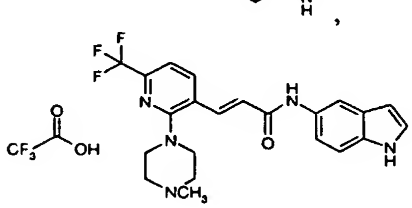
,

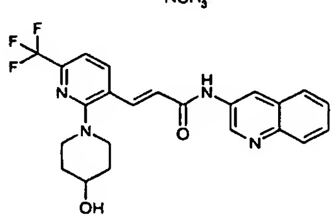
,

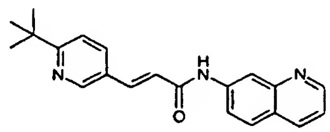
,

,

,

,

,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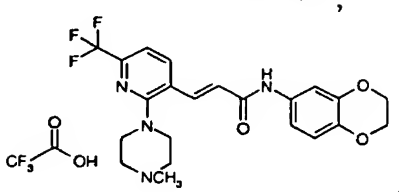
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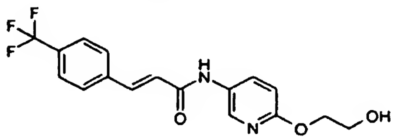
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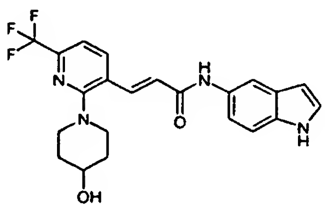
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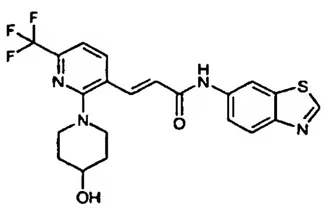
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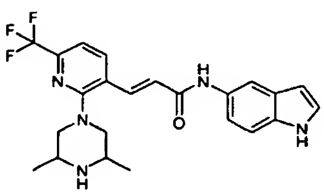
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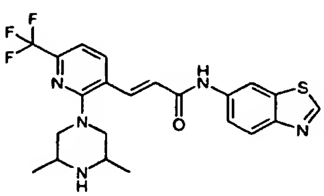
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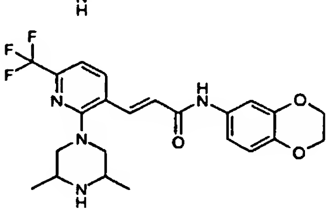
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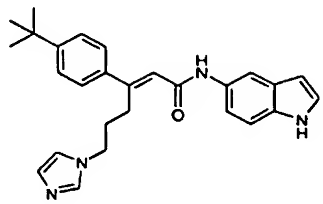
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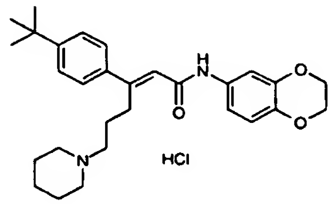
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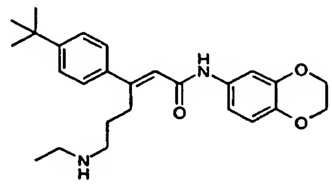
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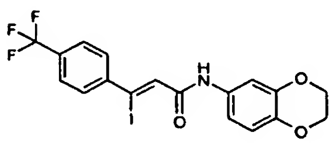
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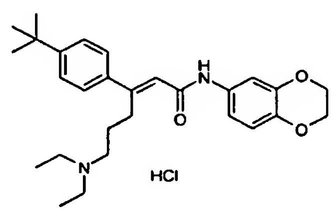
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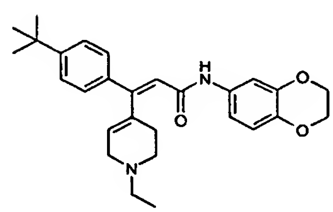
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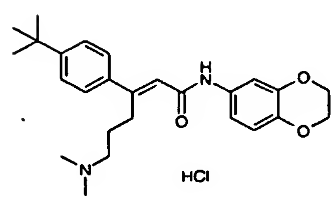
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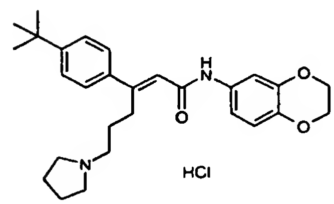
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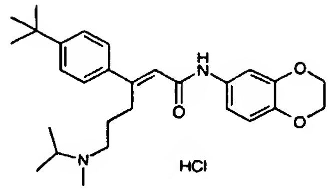
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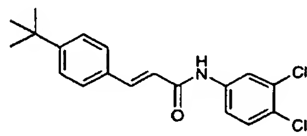
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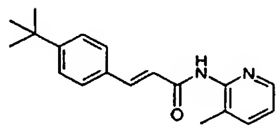
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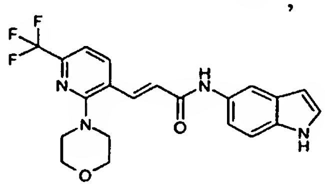
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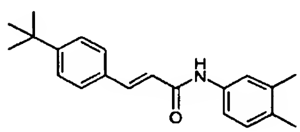
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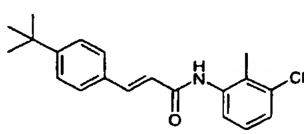
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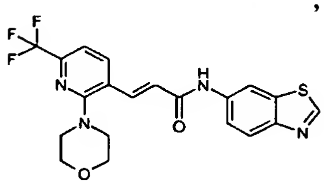
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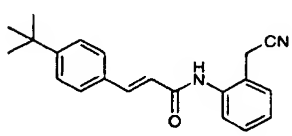
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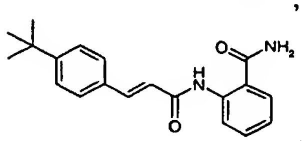
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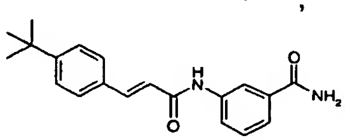
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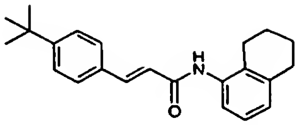
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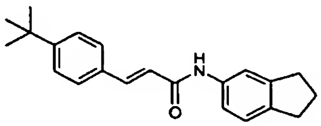
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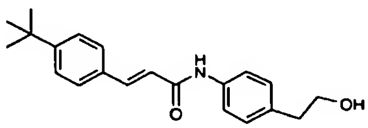
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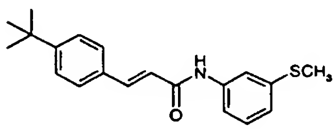
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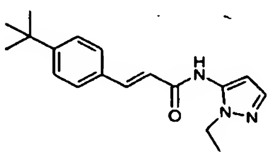
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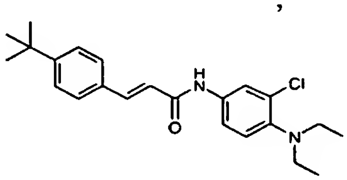
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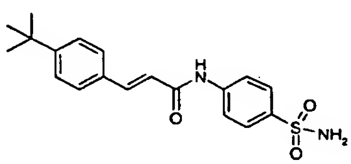
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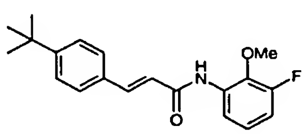
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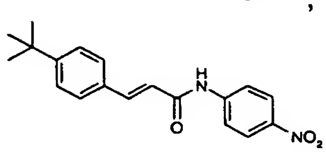
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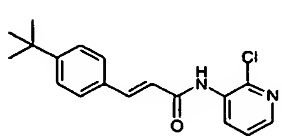
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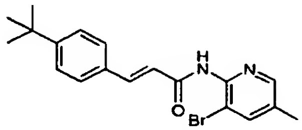
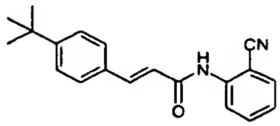
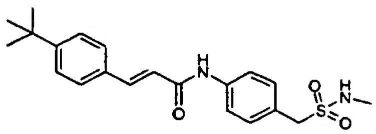
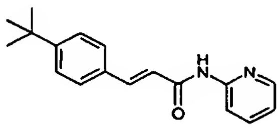
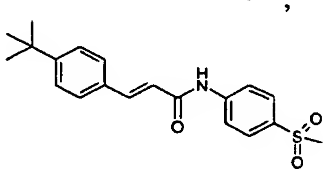
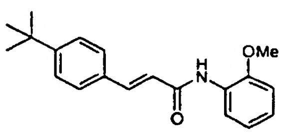
,

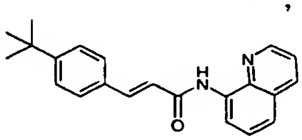
,

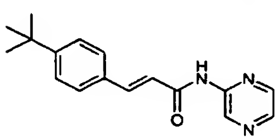
,

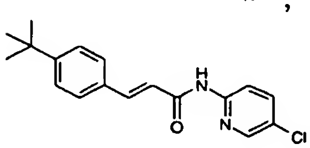
,

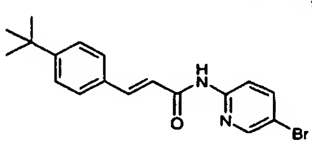
,

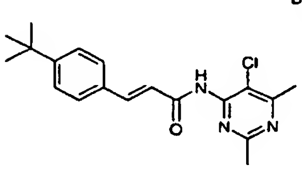
,

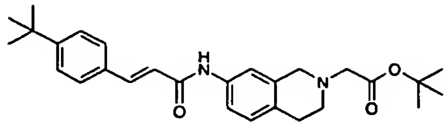
,

,

,

,

,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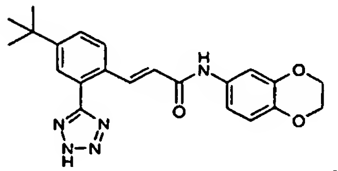
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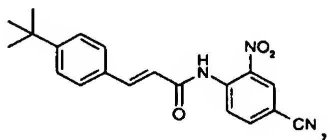
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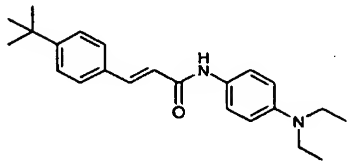
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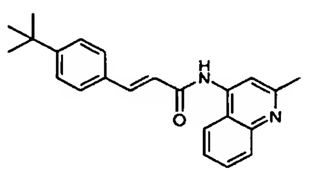
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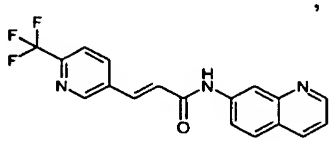
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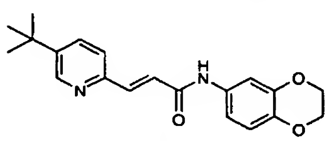
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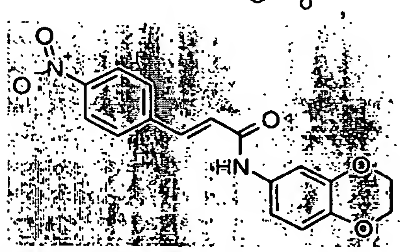
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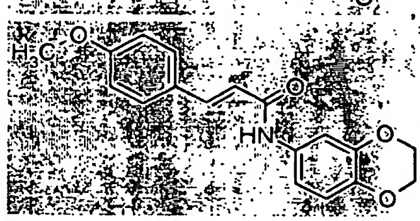
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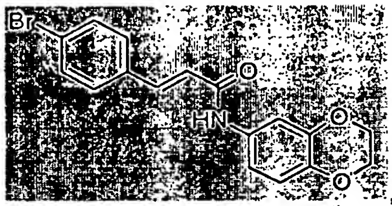
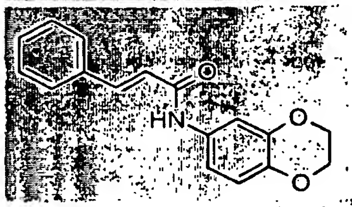
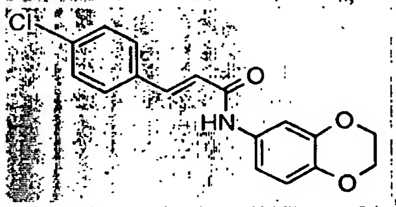
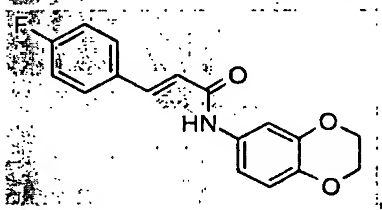
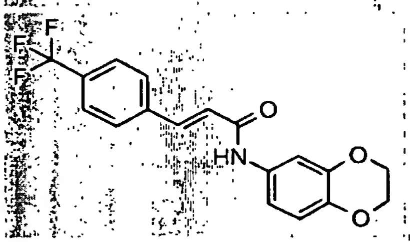
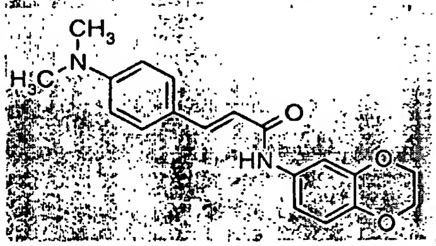
,

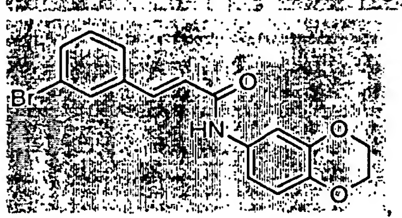
,

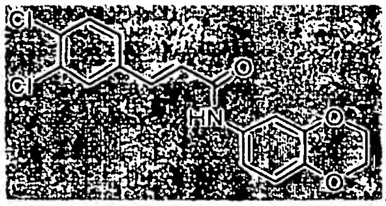






,

,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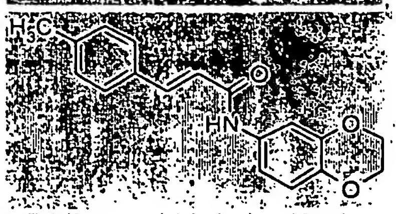
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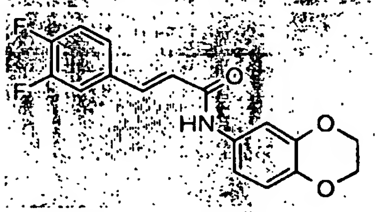
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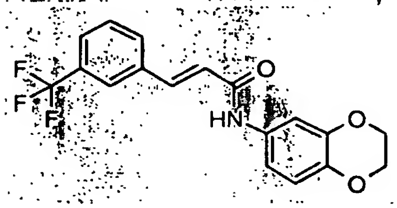
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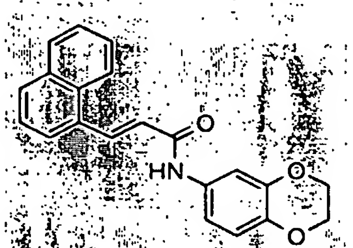
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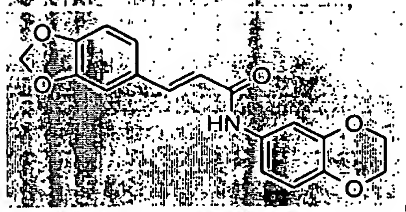
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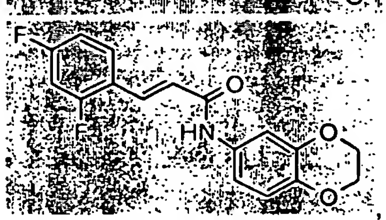
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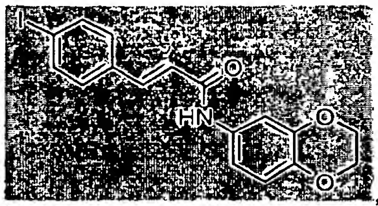
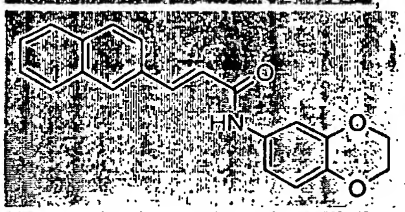
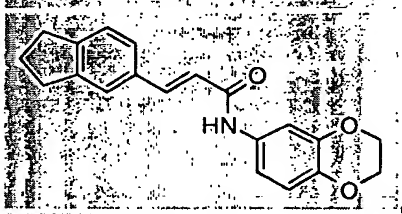
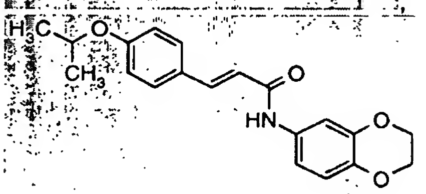
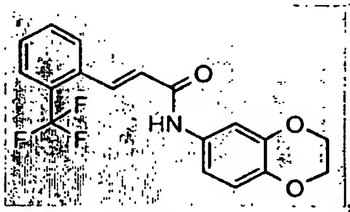
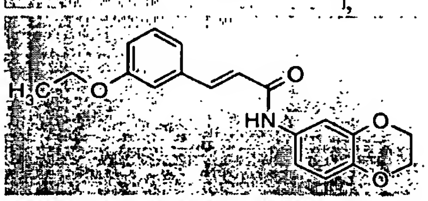
,

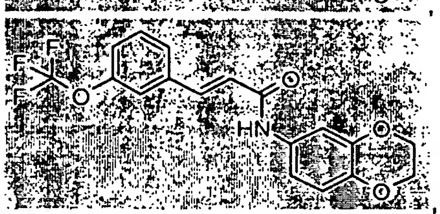
,

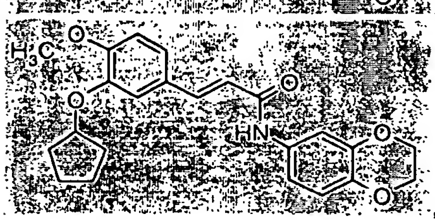
,

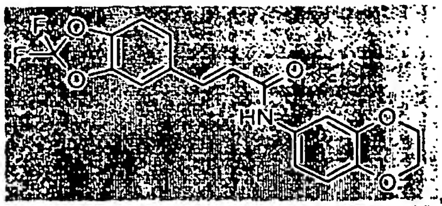
,

,

,

,

,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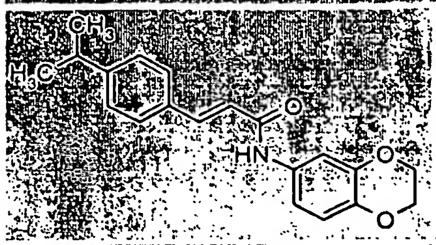
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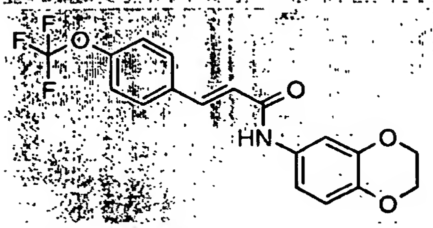
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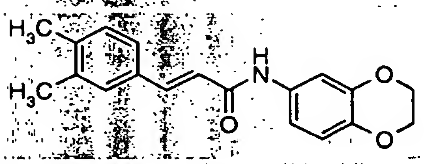
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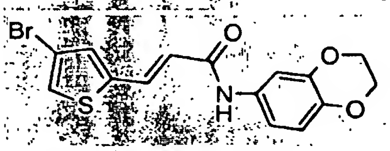
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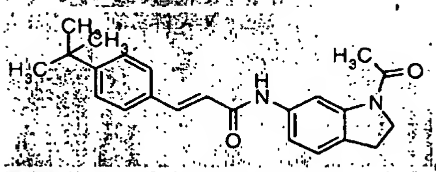
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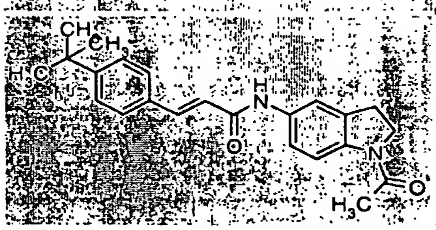
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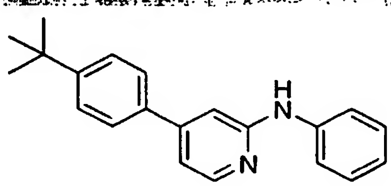
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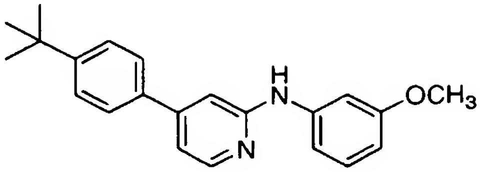
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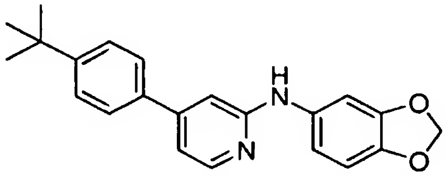
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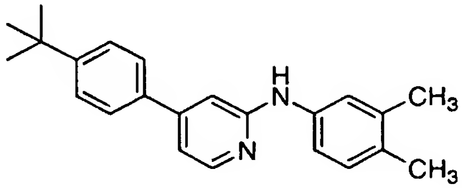
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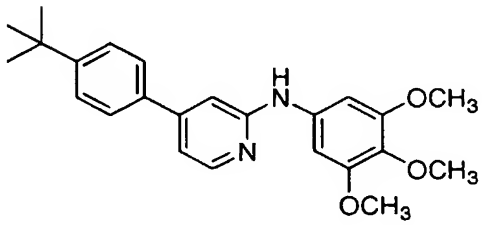
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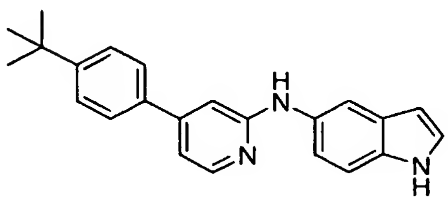
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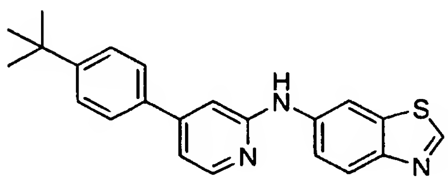
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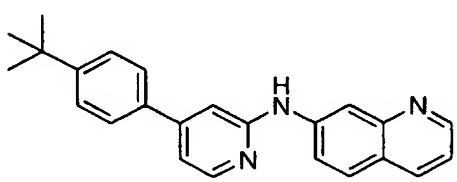
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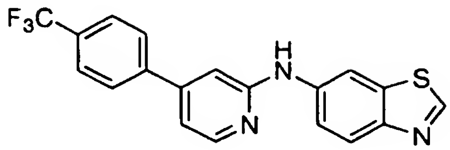

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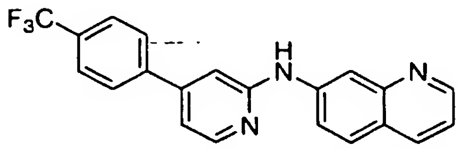

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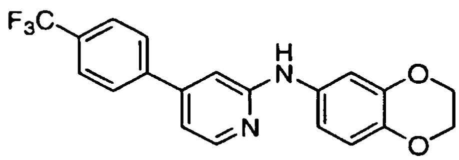

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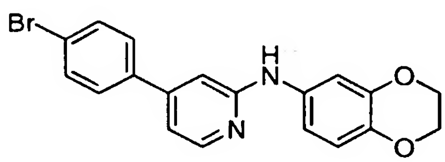

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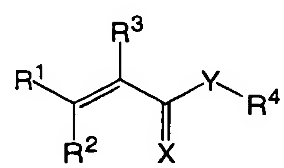
169. A pharmaceutical composition comprising a compound according to any one of Claims 1-168 and a pharmaceutically-acceptable diluent or carrier.

170. The use of a compound according the any one of Claims 1-168 as a medicament.

171. The use of a compound according the any one of Claims 1-168 in the manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex,

disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders.

172. The manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, wherein the medicament contains a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

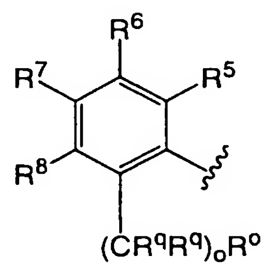
R^3 is H or C_{1-4}alkyl;

R^5 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m;

R^8 is H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the

combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and $-NR^mC_{2-6}$alkylOR^m; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

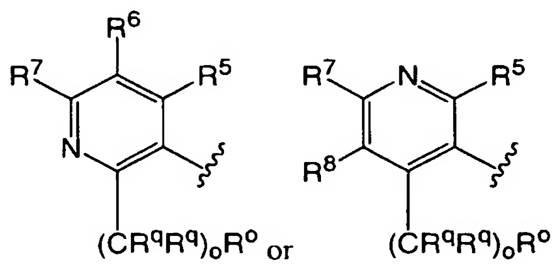
R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m or $-NR^m-C_{1-6}$alkylOR^m;

R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$,

$-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

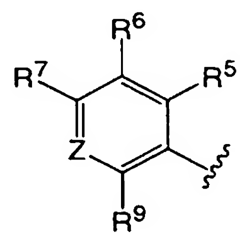
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or

4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}$alkylNR^mR^m, $-O-C_{1-6}$alkylOR^m, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}$alkylNR^mR^m, $-NR^m-C_{1-6}$alkylOR^m, $-C(=O)C_{1-6}$alkyl, $-OC(=O)C_{1-6}$alkyl, $-C(=O)NR^mC_{1-6}$alkyl, $-NR^mC(=O)C_{1-6}$alkyl $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

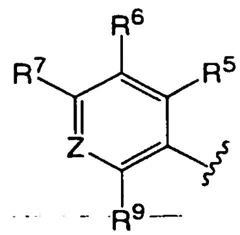
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is C_{1-6}alkyl substituted by 1, 2 or 3 substituents selected from C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$,

$-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$,

-S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and -NR^{m}C$_{2-6}$alkylOR^m;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C$_{1-8}$alkyl, C$_{1-4}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m, -OC$_{2-6}$alkylOR^m, -SR^m, -S(=O)R^n, -S(=O)$_2$R^n, -S(=O)$_2$NR^{m}R^m, -S(=O)$_2$N(R^m)C(=O)R^n, -S(=O)$_2$N(R^m)C(=O)OR^n, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^m, -NR^{m}R^m, -N(R^m)C(=O)R^n, -N(R^m)C(=O)OR^n, -N(R^m)C(=O)NR^{m}R^m, -N(R^m)C(=NR^m)NR^{m}R^m, -N(R^m)S(=O)$_2$R^n, -N(R^m)S(=O)$_2$NR^{m}R^m, -NR^{m}C$_{2-6}$alkylNR^{m}R^m, -NR^{m}C$_{2-6}$alkylOR^m, -C(=O)R^s, -C(=O)OR^s, -C(=O)NR^{m}R^s, -C(=NR^m)NR^{m}R^s, -OR^s, -OC(=O)R^s, -OC(=O)NR^{m}R^s, -OC(=O)N(R^m)S(=O)$_2$R^s, -OC$_{2-6}$alkylNR^{m}R^s, -OC$_{2-6}$alkylOR^s, -SR^s, -S(=O)R^s, -S(=O)$_2$R^s, -S(=O)$_2$NR^{m}R^s, -S(=O)$_2$N(R^m)C(=O)R^s, -S(=O)$_2$N(R^m)C(=O)OR^s, -S(=O)$_2$N(R^m)C(=O)NR^{m}R^s, -NR^{m}R^s, -N(R^m)C(=O)R^s, -N(R^m)C(=O)OR^s, -N(R^m)C(=O)NR^{m}R^s, -N(R^m)C(=NR^m)NR^{m}R^s, -N(R^m)S(=O)$_2$R^s, -N(R^m)S(=O)$_2$NR^{m}R^s, -NR^{m}C$_{2-6}$alkylNR^{m}R^s, -NR^{m}C$_{2-6}$alkylOR^s and C$_{1-4}$alkyl substituted by 1 or 2 groups selected from C$_{1-2}$haloalkyl, halo, cyano, nitro, -C(=O)R^n, -C(=O)OR^n, -C(=O)NR^{m}R^m, -C(=NR^m)NR^{m}R^m, -OR^m, -OC(=O)R^n, -OC(=O)NR^{m}R^m, -OC(=O)N(R^m)S(=O)$_2$R^n, -OC$_{2-6}$alkylNR^{m}R^m,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

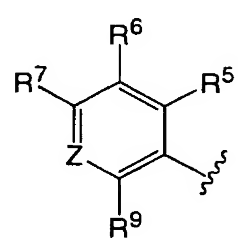
R^7 is $C_{2-8}alkyl$, $C_{1-5}haloalkyl$, I, Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$,

$-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

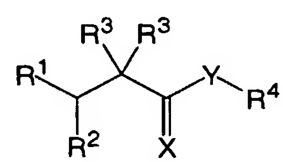
R^7 is $C_{2-6}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

173. The manufacture of a medicament for the treatment of acute, inflammatory and neuropathic pain, dental pain, general headache, migraine, cluster headache, mixed-vascular and non-vascular syndromes, tension headache, general inflammation, arthritis, rheumatic diseases, osteoarthritis, inflammatory bowel disorders, inflammatory eye disorders, inflammatory or unstable bladder disorders, psoriasis, skin complaints with inflammatory components, chronic inflammatory conditions, inflammatory pain and associated hyperalgesia and allodynia, neuropathic pain and associated hyperalgesia and allodynia, diabetic neuropathy pain, causalgia, sympathetically maintained pain, deafferentation syndromes, asthma, epithelial tissue damage or dysfunction, herpes simplex, disturbances of visceral motility at respiratory, genitourinary, gastrointestinal or vascular regions, wounds, burns, allergic skin reactions, pruritis, vitiligo, general gastrointestinal disorders, gastric ulceration, duodenal ulcers, diarrhea, gastric lesions induced by necrotising agents, hair growth, vasomotor or allergic rhinitis, bronchial disorders or bladder disorders, wherein the medicament contains a compound having the structure:



wherein:

X is O, S or NR^m;

n is independently, at each instance, 0, 1 or 2;

o is independently, at each instance, 0, 1, 2 or 3;

R^m is independently at each instance H or R^n;

R^n is independently at each instance C_{1-8}alkyl, phenyl or benzyl;

R^q is independently in each instance H, C_{1-4}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$,

$-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$;

R^s is R^n substituted by 0, 1, 2 or 3 substituents independently selected from R^q;

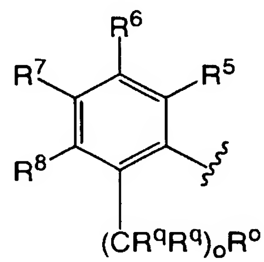
R^3 is H or $C_{1-4}alkyl$;

R^5 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$

R^6 is, independently at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

R^8 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$; and

(A) R^1 is



R^2 is H, $-OR^m$, halo, $C_{1-3}haloalkyl$ or $C_{1-6}alkyl$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$,

$-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

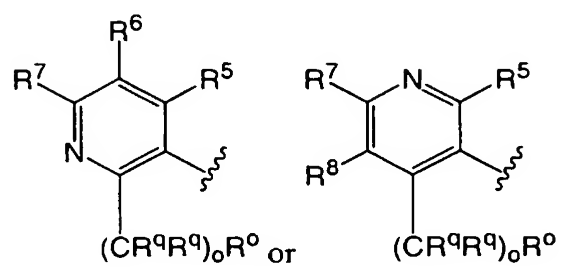
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or

2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(B) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$,

$-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

R^7 is C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}$alkyl, $-O-C_{1-4}$haloalkyl, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}$haloalkyl, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

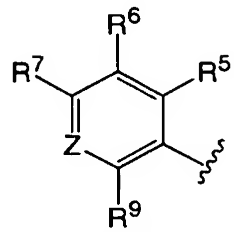
R^o is a saturated, partially-saturated or unsaturated 5-, 6- or 7-membered monocyclic or 7-, 8-, 9-, 10- or 11-membered bicyclic ring containing 0, 1, 2, 3 or 4 atoms selected from N, O and S, so long as the combination of O and S atoms is not greater than 2, wherein the carbon atoms of the ring are substituted by 0, 1 or 2 oxo groups, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from R^p;

R^p is independently at each instance C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$,

$-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$ or $-NR^mC_{2-6}alkylOR^m$; and

Y is O or NH; or

(C) R^1 is



R^2 is H, $-OR^m$, halo, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated, partially-saturated or unsaturated 8-, 9-, 10 or 11-membered bicyclic heterocycle containing 1, 2, 3, 4 or 5 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 2, but excluding quinolin-6-yl, 4,5,6,7-tetrahydro-benzo[b]thiophen-2-yl, benzothiazol-2-yl, 2,3-dihydro-benzo[1,4]dioxin-6-yl, wherein the heterocycle is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-9}alkyl, oxo, C_{1-4}haloalkyl, halo, nitro, cyano, $-OR^m$, $-S(=O)_nC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, $-C(=O)C_{1-6}alkyl$, $-OC(=O)C_{1-6}alkyl$, $-C(=O)NR^mC_{1-6}alkyl$, $-NR^mC(=O)C_{1-6}alkyl$ $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$,

$-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not 2-aminocarbonylmethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, 2-cyanomethyl-2,3-dihydro-benzo[1,4]dioxin-8-yl, quinolin-3-yl, 3H-quinazolin-4-on-3-yl, benzo[1,3]dioxol-5-yl, 3,3-dimethyl-1,3-dihydro-indol-2-on-6-yl or 4,4-dimethyl-3,4-dihydro-1H-quinolin-2-on-7-yl;

R^7 is $C_{1-8}alkyl$, $C_{1-5}haloalkyl$, I or Br

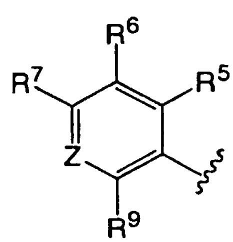
R^9 is H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$, $-NR^m-C_{1-6}alkylOR^m$, or $-(CH_2)_nR^c$;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(D) R^1 is



R^2 is $C_{1-6}alkyl$ substituted by 1, 2 or 3 substituents selected from

C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m or $-NR^mC_{2-6}$alkylOR^m; or

R^2 is $-(C(R^q)_2)_o$phenyl, wherein the phenyl is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-NR^mC_{2-6}$alkylOR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}$alkylNR^mR^s, $-NR^mC_{2-6}$alkylOR^s and C_{1-4}alkyl substituted by 1 or 2 groups selected from C_{1-2}haloalkyl, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}$alkylNR^mR^m, $-OC_{2-6}$alkylOR^m, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}$alkylNR^mR^m, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}$alkylNR^mR^s, $-OC_{2-6}$alkylOR^s, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; or

R^2 is $-(C(R^q)_2)_oR^r$, wherein R^r is a saturated or unsaturated 5- or 6-membered ring heterocycle containing 1, 2 or 3 heteroatoms independently selected from N, O and S, wherein no more than 2 of the ring members are O or S, wherein the heterocycle is optionally fused with a phenyl ring, and the heterocycle or fused phenyl ring is substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$,

$-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S that is optionally vicinally fused with a saturated or unsaturated 3- or 4-atom bridge containing 0, 1, 2 or 3 atoms selected from O, N and S with the remaining atoms being carbon, so long as the combination of O and S atoms is not greater than 2, wherein the ring and bridge are substituted by 0, 1, 2 or 3 substituents independently selected from $C_{1-8}alkyl$, $C_{1-4}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)OR^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$,

$-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$, and the ring and bridge carbon atoms are substituted with 0, 1 or 2 =O groups;

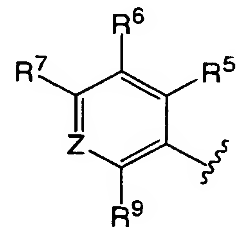
R^7 is C_{2-8}alkyl, C_{1-5}haloalkyl, I, Br;

R^9 is independently, at each instance, H, C_{1-9}alkyl, C_{1-4}haloalkyl, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N; or

(E) R^1 is



R^2 is H, $-OR^m$, Cl, C_{1-3}haloalkyl or C_{1-6}alkyl;

R^4 is a saturated or unsaturated 5- or 6-membered ring containing 0, 1, 2 or 3 atoms selected from O, N and S, so long as the combination of O and S atoms is not greater than 1, wherein the ring is substituted by 0, 1, 2 or 3 substituents independently selected from C_{1-8}alkyl, C_{1-4}haloalkyl, halo, cyano, nitro, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^n$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-NR^mC_{2-6}alkylOR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$,

$-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $C_{1-4}alkyl$ substituted by 1 or 2 groups selected from $C_{1-2}haloalkyl$, halo, cyano, nitro, $-C(=O)R^n$, $-C(=O)NR^mR^m$, $-C(=NR^m)NR^mR^m$, $-OR^m$, $-OC(=O)R^n$, $-OC(=O)NR^mR^m$, $-OC(=O)N(R^m)S(=O)_2R^n$, $-OC_{2-6}alkylNR^mR^m$, $-OC_{2-6}alkylOR^m$, $-SR^m$, $-S(=O)R^n$, $-S(=O)_2R^n$, $-S(=O)_2NR^mR^m$, $-S(=O)_2N(R^m)C(=O)R^n$, $-S(=O)_2N(R^m)C(=O)OR^n$, $-S(=O)_2N(R^m)C(=O)NR^mR^m$, $-NR^mR^m$, $-N(R^m)C(=O)R^n$, $-N(R^m)C(=O)OR^n$, $-N(R^m)C(=O)NR^mR^m$, $-N(R^m)C(=NR^m)NR^mR^m$, $-N(R^m)S(=O)_2R^n$, $-N(R^m)S(=O)_2NR^mR^m$, $-NR^mC_{2-6}alkylNR^mR^m$, $-C(=O)R^s$, $-C(=O)OR^s$, $-C(=O)NR^mR^s$, $-C(=NR^m)NR^mR^s$, $-OR^s$, $-OC(=O)R^s$, $-OC(=O)NR^mR^s$, $-OC(=O)N(R^m)S(=O)_2R^s$, $-OC_{2-6}alkylNR^mR^s$, $-OC_{2-6}alkylOR^s$, $-SR^s$, $-S(=O)R^s$, $-S(=O)_2R^s$, $-S(=O)_2NR^mR^s$, $-S(=O)_2N(R^m)C(=O)R^s$, $-S(=O)_2N(R^m)C(=O)OR^s$, $-S(=O)_2N(R^m)C(=O)NR^mR^s$, $-NR^mR^s$, $-N(R^m)C(=O)R^s$, $-N(R^m)C(=O)OR^s$, $-N(R^m)C(=O)NR^mR^s$, $-N(R^m)C(=NR^m)NR^mR^s$, $-N(R^m)S(=O)_2R^s$, $-N(R^m)S(=O)_2NR^mR^s$, $-NR^mC_{2-6}alkylNR^mR^s$, $-NR^mC_{2-6}alkylOR^s$ and $-NR^mC_{2-6}alkylOR^m$; wherein R^4 is not unsubstituted phenyl;

R^7 is $C_{2-6}alkyl$, $C_{1-5}haloalkyl$, I or Br;

R^9 is independently, at each instance, H, $C_{1-9}alkyl$, $C_{1-4}haloalkyl$, halo, nitro, cyano, $-OC_{1-6}alkyl$, $-O-C_{1-4}haloalkyl$, $-O-C_{1-6}alkylNR^mR^m$, $-O-C_{1-6}alkylOR^m$, $-NR^mR^m$, $-NR^m-C_{1-4}haloalkyl$, $-NR^m-C_{1-6}alkylNR^mR^m$ or $-NR^m-C_{1-6}alkylOR^m$;

Y is NH; and

Z is CR^8 or N.

174. A pharmaceutical composition comprising a compound according to any one of Claims 1-168 and a pharmaceutically-acceptable diluent or carrier.

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(75) Inventors/Applicants *(for US only)*: **BO, Yunxin, Y.** [CN/US]; 419 Calle Veracruz, Thousand Oaks, CA 91320 (US). **CHAKRABARTI, Partha, P.** [IN/US]; 521 Yarrow Drive, Simi Valley, CA 93065 (US). **CHEN, Ning** [CN/US]; 2342 Gillingham Circle, Thousand Oaks, CA 91362 (US). **DOHERTY, Elizabeth, M.** [US/US]; 284 Marjori Avenue, Newbury Park, CA 91320 (US). **FOTSCH, Christopher, H.** [US/US]; 533 Timberwood Avenue, Thousand Oaks, CA 91360 (US). **HAN, Nianhe** [US/US]; 2217 Rutland Place, Thousand Oaks, CA 91362 (US). **KELLY, Michael, G.** [GB/US]; 790 Sandoval Place, Thousand Oaks, CA 91360 (US). **LIU, Qingyian** [CN/US]; 4631 Paseo Girasol, Camarillo, CA 93012 (US). **NORMAN, Mark, Henry** [US/US]; 130 Venus Street, Thousand Oaks, CA 91360 (US). **WANG, Xianghong** [CN/US]; 11621 Country Springs Ct., Moorpark, CA 93021 (US). **ZHU, Jiawang** [US/US]; 77 Mahogany Lane, Simi Valley, CA 93065 (US).

(74) Agents: **ODRE, Steven M.** et al.; Amgen Inc., One Amgen Center Drive, M/S 27-4-A, Thousand Oaks, CA 91320-1799 (US).

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(84) Designated States *(regional)*: ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG).

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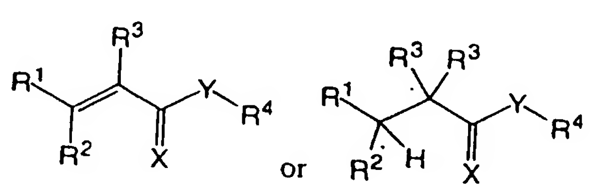
(54) Title: VANILLOID RECEPTOR LIGANDS AND THEIR USE IN TREATMENTS



(57) Abstract: Compounds having the general structure of the Formula (I) and compositions containing them, for treatment of various diseases.

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INTERNATIONAL SEARCH REPORT

International application No.

PCT/US02/39589

A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C07C 233/11; C07D 403/12, 413/12, 417/12, 265/36, 241/40; A61K 31/4418, 31/47, 31.489, A61P 31/12, 3

US CL : 562/234; 544/106,353; 546/268.1, 282.7, 134; 548/152; 514/231.2, 249, 311, 336, 443

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. :

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

CASONLINE, EAST

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 4,753,934 A (NICKL et al) 28 June 1988 (28.06.1988), see entire document, especially column 9 through column 43 for compounds.	1-20, 80-166, 168, 172, 173
X	US 3,940,422 A (HARITA et al) 24 February 1976 (24.02.1976), see entire document especially examples 1-67.	1-20, 80-166, 168, 172, 173
X	US 3,853,561 A (REICHEL et al) 10 December 1974 (10.12.1974), see entire document especially examples 1-7.	1-20, 80-166, 168, 172, 173
X	JP 63 154663 A (KANEGAFUCHI CHEM IND CO LTD) 27 June 1988 (27.06.1988), see entire docummment, especially pages 568-563 for compounds.	1-20, 80-166, 168, 172, 173
X,P	US 2003/0087922 A1(BETHIEL et al) 08 May 2003 (08.05.2003).	21-55, 167

☐ Further documents are listed in the continuation of Box C. ☐ See patent family annex.

* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
28 June 2003 (28.06.2003)	04 AUG 2003
Name and mailing address of the ISA/US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703)305-3230	Authorized officer Venkataraman Balasubramanian Telephone No. (703)308-1235

Form PCT/ISA/210 (second sheet) (July 1998)

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US02/39589

Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

2. ☐ Claim Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:

3. ☒ Claim Nos.: 169,170,171 and 174
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:

4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.
☐ No protest accompanied the payment of additional search fees.

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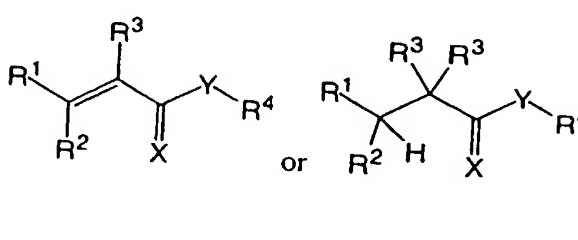

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